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## Stroke survivors', caregivers' and GPs' attitudes towards a Polypill for the secondary prevention of stroke: A qualitative interview study

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3 Stroke survivors', caregivers' and GPs' attitudes towards a  
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6 Polypill for the secondary prevention of stroke: A qualitative  
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10 interview study  
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## ABSTRACT

### Objectives

To understand survivors of stroke or transient ischaemic attack, caregivers and GPs perspectives and beliefs on a polypill approach, consisting of blood pressure lowering and cholesterol lowering therapies, with or without aspirin, for the secondary prevention of stroke.

### Methods

A qualitative interview study was undertaken within GP surgeries in the East of England. Twenty-eight stroke survivors were interviewed, 14 jointly with a caregiver, along with 5 GPs responsible for their care. Interview topic guides explored attitudes to a polypill, factors likely to influence uptake and long term use, management of polypill medication and factors influencing the decision to prescribe polypill. Data were analysed using a grounded theory approach. Key themes are presented and augmented with verbatim quotes.

### Results

Overall study participants were positive about the polypill concept and considered it acceptable in the treatment of stroke. Benefits of polypill identified included convenience leading to improved adherence and reduced burden of treatment. Caregivers felt it would improve medication taking practices and GP were open to prescribing it to those at risk. However, concerns raised included whether a polypill providing equivalent therapeutic benefit, side effects through combining medications, consequences of nonadherence, lack of flexibility in regulating dosage, disruption to current treatment and suitability to the wider stroke population.

## Conclusion

Participants supported this treatment approach for the secondary prevention of stroke, however, significant concerns around a polypill strategy remain. Further research on the efficacy of polypill is needed to reassure practitioners whose concerns around inflexibility and the suitability of treatment are likely to influence the decision to prescribe a polypill for secondary stroke prevention. Acceptability of this treatment approach among patients, caregivers and GPs is likely to determine the uptake and subsequent use of a polypill as a treatment for stroke in the future.

Key words: Polypill, Stroke, Qualitative research, Semi-structured interview

Abbreviations: FDC: Fixed-dose combination; CVD: Cardiovascular disease.

## Article summary

### Article focus

- Cholesterol lowering and blood pressure lowering therapies as well as aspirin, can substantially reduce long term risk following a stroke event.
- A polypill consisting of multiple medications in a single tablet has been advocated as a treatment for the prevention of cardiovascular disease including stroke.
- The aim of this investigation was to explore the views and attitudes of survivors, caregivers and general practitioners, towards a polypill approach for the secondary prevention of stroke.

### Key messages

- A polypill was considered acceptable, offering greater convenience and the potential to improve medication adherence in stroke survivors.
- Participants expressed concerns around treatment inflexibility, the suitability of polypill for everyone and the potential for medication side effects.
- Addressing the concerns of survivors, caregivers and GPs will be key to implementing a polypill approach in the future.

### Strengths and limitations

- This research adds to an important body of work exploring cardiovascular polypills and is the first study to focus on attitudes to a polypill for stroke prevention.
- The findings are strengthened by the inclusion of caregivers who have an important role to play in managing the medication of stroke survivors.
- Conducting a qualitative assessment of individual perspectives allowed an in-depth and robust examination of the subject area.
- Due to the limited sample size findings may not generalise to the wider stroke population or necessarily represent the views of all health professionals.
- Future research should consider harder to reach groups such as those who need support to manage medication and who may benefit most from the polypill approach.

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## INTRODUCTION

Stroke is the fourth most common cause of death in the UK, responsible for approximately 40,000 deaths every year<sup>1</sup> and is also a significant cause of acquired adult disability<sup>2</sup>, with about half of all survivors experiencing some degree of physical or cognitive impairment<sup>3</sup> and left dependent on others<sup>4</sup>.

People who have had a stroke or a transient ischaemic attack (TIA) also known as a mini-stroke are at high long term risk of a further event<sup>5-6</sup>, however, this can be substantially reduced through the use of preventative medications such as anti-platelet agents<sup>7</sup> or anticoagulants<sup>8</sup>, as well as cholesterol lowering<sup>9-10</sup> and blood pressure (BP) lowering therapies<sup>11</sup>.

Despite evidence based guidelines, treatment for stroke often falls below recommended standards<sup>12-13</sup> and significant deficiencies in secondary prevention care have been reported<sup>14</sup>.

The use of multiple medications to treat CVD is often associated with inappropriate medication use (e.g. under use or use of non-appropriate medicines), under prescription and reduced adherence<sup>15</sup>. A polypill consisting of cholesterol lowering and blood pressure lowering therapies, with or without aspirin in a single pill for the treatment of CVD<sup>16</sup> has been proposed.

Wald and Law (2003) introduced the concept and estimated a theoretical 88% reduction in ischaemic heart disease and 80% reduction in stroke, if taken by everyone over 55<sup>17</sup>. Since then a growing body of literature has developed around fixed-dose combination (FDC) or polypill strategy for the prevention of cardiovascular disease<sup>18-19</sup>.

However less is known about patients or practitioners attitudes towards a polypill strategy. To date a small number of investigations have been completed. Although patients considered it

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2  
3 convenient, there were concerns around inflexibility of treatment <sup>20</sup> and GPs would consider  
4 prescribing it to those in need if it was shown to be effective. <sup>21-24</sup> With adherence to  
5 medication in stroke survivors known to be suboptimal <sup>25</sup>, this group may be particularly  
6 suited to treatment via a FDC polypill.  
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11  
12 The aim of this study was to explore the attitudes and perspectives of stroke/TIA survivors,  
13 carers and GPs towards a polypill approach for the secondary prevention of stroke including  
14 the benefits and consequences of using a polypill, factors likely to influence polypill uptake,  
15 the caregiver role in managing medication and GPs views and attitudes towards prescribing a  
16 polypill in the future.  
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## 27 **METHODS**

### 28 **Study Design and Participants**

29  
30 A qualitative study using semi-structured interviews. Purposive sampling was used to recruit  
31 participants with maximum variety characteristics representing a spread of socio-economic  
32 status <sup>26</sup>, age, gender, and disability <sup>27</sup>. A search of the GP practice stroke register identified  
33 all patients over the age of 55, with a stroke or TIA. Every 3<sup>rd</sup> patient was selected from the  
34 practice, screened for suitability and approached by letter in batches of 25. Interview  
35 saturation was reached when no new information emerged from discussions. Carers were  
36 approached via stroke survivor and interviews were arranged by phone with the lead GP at  
37 each practice. Ethical approval was granted by NHS South Yorkshire Research Ethics  
38 Committee, Ref 13-YH-0067.  
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### 51 **Data Collection**

52  
53 Data was collected through semi-structured interviews with open ended questions that  
54 defined the area to be explored <sup>28</sup>. Topic guides were piloted with 2 stroke survivors and  
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checked by a GP and appropriate recommendations implemented. All interviews were conducted by the lead author, JJ, who has considerable experience in qualitative research analysis. Field notes were also taken by the interviewer. The schedule of questions was refined and finalised after the 5th interview. Topics discussed were perceived benefits and consequences of a polypill, factors influencing polypill uptake, caregiver views and GPs beliefs and attitudes towards prescribing polypill. Interviews were audiotaped, lasted 1- 1.5 hours and were transcribed verbatim.

### Data analysis

Analysis followed a grounded theory approach with constant comparative analysis<sup>29</sup>. A set of codes representing initial themes were developed and refined throughout the data analysis phase. Codes were grouped into similar concepts and from these codes categories were formed. The process of identification and refinement of categories continued until the final themes emerged. Nvivo 9 (QSR Intl, Melbourne, Victoria, Australia) was used to organise, code and manage the data. Transcripts were entered in to the program and coded by JJ, with 20% double coded independently by SS. Queries arising from coded transcripts were settled through discussion. Communication with a third author (JG) enabled clarification and refinement of categories until a consensus on the final themes was reached.

## RESULTS

Twenty-eight stroke survivors participated. Fourteen were interviewed alone and 14 with the caregiver present, who was either a spouse (n=12) or family member (n=2). Characteristics of stroke survivors are displayed in Table 1 below. Three male GPs and two female GPs were also interviewed. One GP was white British, one was Chinese and three were of south Asian origin.



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4  
5 Table 1 here.  
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8

### 9 10 **Polypill benefits**

#### 11 **Convenience**

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13  
14 Participants were enthusiastic about one tablet combining all stroke medication and reducing  
15  
16 treatment burden through minimising the inconvenience of managing multiple medications.  
17

18  
19  
20  
21 That is the best thing I've read when it said you might have to take one pill to cover  
22  
23 the lot. Super, because that is just a bugbear, it's a bugbear in life. (pp 11, Male,  
24  
25 73yrs).  
26  
27

28  
29  
30 A single tablet was considered easier to remember and likely to improve overall medication  
31  
32 taking behaviour.  
33  
34

35  
36  
37 I think it's brilliant because erm I, I've got more chance of remembering to take one  
38  
39 tablet than I have of remembering two different times of the day if you like. (pp10,  
40  
41 Male, 66 yrs)  
42  
43

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45  
46 While GPs also felt polypill had the potential to improve medication adherence.

47  
48 I think that would reduce the pill burden to our patients and I think that's very good  
49  
50 idea [ ]...[ ] I think he would be very compliant with it, because he is thinking that  
51  
52 he is going to be taking 1 tablet and not 5 tablets....(GP 02, Female).  
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3 The potential for 'cross-over' treatment in individuals with multiple existing cardiovascular  
4 co-morbidities was mentioned.  
5

6  
7 if you're giving polypill in the form of one pill, even with people with comorbidities  
8 (you're) maybe reducing their number [ ] and might improve overall compliance  
9 and it may have the side effect of improving their comorbidity as well (GP 05, Male).  
10  
11  
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15  
16 Carers agreed that a polypill made the medication taking process less demanding.  
17

18  
19  
20 It's logic to me and I think it's an excellent idea if it could be done, certainly instead  
21 of Jean fiddling about in a saucer trying to pick up tablets.. (pp28, Male, carer).  
22  
23  
24

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26  
27 They also felt that the process of obtaining and managing medication was better compared  
28 with using multiple medications.  
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30  
31

32  
33  
34 One tablet is good really isn't it, because it means that you if you've taken that one  
35 you've taken them all. Whereas sometimes if you run short, you think oh I'll just take  
36 that and forget about the other one until you go the doctors and get the refill. (pp02,  
37 Female, Carer)  
38  
39  
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45 Benefits of correct treatment

46  
47 Polypill offered the benefit of correct medication and it ensured the patient received all of  
48 their recommended medications.  
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50

51  
52 It could protect, once you had polypills that contained a mixture of medications  
53 which are known not to have...contradictory side-effects...then you would feel very  
54 safe. (pp03, Male, 86 yrs)  
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5 There was also confidence that components were safe, tested and therefore provided the most  
6  
7 appropriate treatment.  
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10  
11 I'm all for these things.. [ ] it might not be good for you, It might not, I don't know I  
12  
13 can't see how because if they're now gonna put four different pills into one they  
14  
15 musta investigated a, b, c and d to put them in one so therefore it's going to be  
16  
17 beneficial to me and anybody else that wants those four in one (pp11, Male, 73yrs).  
18  
19

### 20 21 22 23 **Polypill concerns**

#### 24 25 26 27 **Appropriateness of treatment**

28  
29 For many survivors an important polypill characteristic was its ability to sustain equivalent  
30  
31 therapeutic benefit while reducing treatment burden.  
32  
33

34  
35  
36 It's a no brainer as far as I'm concerned you've got one tablet with all the ingredients  
37  
38 of the others.. if I've got the same erm dosage of statin and if it didn't disturb my  
39  
40 readings then yeah I mean erm what are the objections to it? (pp05, Male, 64 yrs)  
41  
42  
43

44  
45 However, the prospect of a 'pill for all', inability to alter dosage and being less amenable to  
46  
47 dose titration, if that was required, was frequently questioned.  
48  
49

50  
51  
52 Would the polypill be in different strengths because like for blood pressure at the  
53  
54 moment I'm taking...12 and a half, and then me cl- clopidogrel is 75 [ ], maybe six  
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3 months down the line my blood pressure can reduce, what would that do with the  
4  
5 polypill? (pp21, Female, 68 yrs)  
6  
7

8  
9  
10 Survivors accustomed to scheduled medication regimens also questioned how drugs could  
11  
12 now be combined and taken at a single time point.  
13

14 if you've got them altogether and you're supposed to take those tablets at different  
15  
16 times of the day, how's it going to work? Is it going to upset your system? (pp22,  
17  
18 Female, 71 yrs).  
19

20  
21  
22  
23 Suitability of the polypill strategy

24  
25 Patients questioned the ease of managing treatment if one or more component was no longer  
26  
27 required.  
28

29  
30 Would it only be suitable for somebody who's taking four of that particular  
31  
32 medication? But what would happen if say the Dr said, you're not so bad so you  
33  
34 don't need to take that particular tablet? (pp16, Female, 82 yrs)  
35

36  
37  
38 A few expressed concerns around the inclusion of statins in any combination pill.  
39

40  
41  
42  
43 Yes has that got anything to do with statins? I've read a lot about statins and I'm  
44  
45 afraid I feel I wouldn't want to take them. Because the side effects and everything.  
46  
47 (pp19, Female, carer)  
48

49  
50  
51  
52 GPs were cautious, suggesting polypill could be better suited to those on similar medications  
53  
54 whose treatment was well-established.  
55

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2  
3 I think the right drugs in the right combinations there, it, would potentially be helpful  
4  
5 for a cohort of people. I don't think it will be for everyone but there will be a cohort  
6  
7 of people who will probably be on very similar drugs..[ ] (GP03, Male)  
8  
9

10  
11 Patients and carers were also concerned that poor adherence would lead to patients missing  
12  
13 all of their secondary prevention drugs.  
14

15  
16 if you're gonna give them a polypill that is three or four tablets and they don't bother  
17  
18 taking that..They're gonna be worse off (pp14, Male, Carer)  
19  
20

21  
22 Given the unique needs of stroke patients, some survivors suggested multiple polypills may  
23  
24 be needed.  
25  
26  
27

28  
29 They don't give me three separate ones for no reason, there must be a reason for it.  
30  
31 You can't do that with a polypill unless you have a hundred polypills all different  
32  
33 medications and different combinations (pp18, Male, 88 yrs).  
34  
35  
36

### 37 38 Polypill side effects

39  
40 The likelihood of polypill side effects led many to question the suitability of single pill  
41  
42 treatment.  
43  
44

45  
46  
47 The fine tuning takes a bit of doing so w- with the one pill I got my bit of a doubt that  
48  
49 it might work for some people but it might not work for everybody you see (pp04,  
50  
51 Male, 80 yrs).  
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3 For GPs, a further problem resulting from this was the potential difficulty in identifying the  
4  
5 polypill component responsible for side effects.  
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9  
10 My personal anxiety is about side effects when you club two, three medicines  
11  
12 together, if one of them, one of the components is, is causing the side effect then  
13  
14 you'll not know, you may have to again change.. (GP 05, Male)  
15  
16

### 17 Medication adjustment

18  
19  
20 GPs questioned the benefit in altering established medication routines, to accommodate a  
21  
22 polypill, in those who were already taking their medication as directed.  
23  
24

25 If you've got , as I said, a very motivated patient they are happy with what they are  
26  
27 taking, then we don't probably have to intervene, but we may have to give to people  
28  
29 who are not that motivated or compliant. (GP 05, Male)  
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33  
34 They also expressed concern around the inconvenience of having to re-adjust future treatment  
35  
36 if polypill components were no longer required.  
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40  
41 If somebody has a problem ok well we'll just stop using the polypill and give them  
42  
43 the individual ones but with that stopping and chopping and changing people will say  
44  
45 they've changed my tablets again, that becomes an issue. (GP 04, Male)  
46  
47

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49  
50 However inflexibility of polypill and the inability to manipulate dosage was perhaps the  
51  
52 greatest concern among GPs.  
53

54 We do switch around quite a bit different brands, different sizes, statins and  
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56 sometimes it may not be the right dose but you kind of slowly edge it in..[ ] It would  
57  
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3 be advantageous if it was a single pill but that would be maybe a bit difficult with  
4  
5 polypill.[ ] It's the fine tuning that's difficult..(GP 01, Female)  
6  
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8

9  
10 Size of polypill

11 Health professionals raised concerns that a large pill could actually discourage patients from  
12  
13 taking their medications.  
14

15  
16 Yeah is it a horse tablet? ...that's going to have the other, the opposite effect on  
17  
18 compliance that we want.[ ] People are going to start breaking it having half now and  
19  
20 half twelve hours later..(GP 04, Male).  
21  
22  
23

24  
25 Cost of polypill

26  
27 The burden of polypill on NHS resources was also raised with a number of GPs suggesting a  
28  
29 more expensive pill could be difficult to prescribe.  
30  
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32

33  
34 If it is cheaper then there won't be an issue at all. if it comes out to be more  
35  
36 expensive than the four tablets which you are giving individually to the patient  
37  
38 then it comes to be an issue (GP 02, Female)  
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41

42  
43 Cost implications for practices and pharmacies dispensing polypill were also considered with  
44  
45 GPs acknowledging the likelihood of reduced revenues associated with a single pill.  
46  
47  
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49  
50 They get an item fee for each thing they prescribe so if you have 4 drugs you get a  
51  
52 fee for each, if you put it in 1 pill that will account for one (GP 04, Male)  
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## Polypill lessons for implementation

Although stroke survivors were generally positive about the polypill approach, many were non-committal on its future use, largely due to a lack of existing polypill evidence.

### Polypill recommendation

Many patients felt future polypill use was likely to depend on their doctor recommending the treatment.

It sounds good but w- we've got to, we would have to weigh up, listen to what the doctors say and the consultants and see what history, because this polypill, from what we've hear. Very, very little, it's quite new, that's all we know. (pp22, Male, carer)

### Satisfied with current medication

Being content with their current medication also made survivors less enthusiastic given that potentially negative impacts of polypill use were largely unknown.

Why take a tablet that perhaps will affect you. Plus the fact I'm perfectly happy with what I'm on, you know, at the moment anyway (pp01, Female, 71 yrs).

### Endorsement of polypill

GPs agreed that if they endorsed polypill, stroke survivors were likely to accept it as a treatment for secondary stroke and commit to using it in the future.



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2  
3 I think the majority of our current patients if we told them we think this is the right  
4  
5 thing to do would probably be happy with that. It's a fairly easy argument (GP 03,  
6  
7 Male).  
8  
9

10  
11  
12 And there was an obligation to try new and innovative treatments like the polypill, if its  
13  
14 potential benefits were proven.  
15

16  
17  
18 I welcome change and innovation I'm excited by it... you don't know until you've  
19  
20 tried it. [ ] We have to try it if there was a potential benefit there for people (GP04,  
21  
22 Male)  
23  
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## 28 DISCUSSION

### 29 30 31 **Summary of main findings**

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33  
34 Participants were largely enthusiastic about the polypill concept, representing an  
35  
36 improvement in the medication taking process and management of treatment, greater  
37  
38 convenience, reduced the pill burden and was likely to lead to better medication adherence.  
39  
40 Polypill also ensured patients received the correct treatment and that medications were safe.  
41  
42 Concerns around suitability for everyone, the potential for side effects and limitations of  
43  
44 adjusting dosage and polypill inflexibility, persisted. GPs felt a more expensive pill would be  
45  
46 problematic and acknowledged their endorsement was key to it being accepted by patients.  
47  
48 For survivors the decision to use a polypill depended on the GPs recommendation, however,  
49  
50 those who were satisfied with their current treatment regimen felt less inclined to change to a  
51  
52 polypill approach.  
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## Strengths and Limitations

A strength of this study is that it adds to a growing and important body of research on attitudes towards a cardiovascular polypill with a focus on secondary prevention of stroke. Secondly, this study benefits from a robust methodological approach using semi-structured interviews which permits a robust and in depth assessment of individual perspectives. A further strength is the inclusion of caregivers, who can make a significant contribution in the future management of polypill treatment. We believe the completion of interviews by a qualitative researcher rather than a health professional facilitated a willingness among patients to engage in discussion with survivors welcoming the opportunity to discuss experiences around stroke and preventative treatment. However limitations to consider include a relatively small sample recruited from 5 general practice surgeries. Whilst every effort was made to recruit a representative sample with varied disability, participants were largely a convenience sample consisting of those who responded to our request to participate. In addition, survivors were almost exclusively White British. With some ethnic groups, particularly south Asians, known to be at considerably higher risk of cardiovascular disease<sup>30</sup>, the study may have benefited from the views and attitudes of those individuals who are considered to be at a greater potential risk from stroke and likely to be prospective users of polypill therapy. As a result, study participants may not necessarily represent the wider population. With all caregivers interviewed in the presence of a survivor, this may have contributed to individuals responding in a socially desirable manner. Our aim was to recruit a maximum variety sample however most participants were able bodied and independently managed their own medication. Investigating a polypill among survivors with significant symptoms and dependent on others to organise tablets may be an area for future research in the field. Finally, with a recruitment rate of 6% in the most deprived area we visited further

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3 research should aim for those harder to reach groups of survivors who may benefit most  
4  
5 from a polypill treatment approach.  
6  
7

### 8 **Comparisons with existing literature**

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11 The inflexibility of treatment and the potential for side effects were considered key  
12  
13 challenges for the polypill approach. Concerns around side effects are well founded, having  
14  
15 previously been identified as influencing medication taking behaviour<sup>31</sup> and recognised as a  
16  
17 significant barrier to adherence in cardiovascular disease medication<sup>32</sup>. Our findings are also  
18  
19 in line with a recent UK primary care investigation in which patients considered a secondary  
20  
21 prevention polypill acceptable, but were concerned about components interacting and  
22  
23 inflexibility of treatment<sup>33</sup>. The inability to adapt polypill dosage and the suitability of fixed  
24  
25 dose treatment for stroke survivors was a key concern for GPs in our study and has been  
26  
27 previously reported in studies exploring polypill attitudes among GPs elsewhere. A small  
28  
29 survey of 17 practitioners in New Zealand reported that having no choice of polypill  
30  
31 components or doses was the thing GPs disliked most about the concept of a polypill<sup>21</sup>. In  
32  
33 another UK study of primary healthcare professionals, inability to titrate dosage was  
34  
35 considered a major disadvantage of polypill<sup>24</sup>.  
36  
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41 GPs agreed that cost was a potential impediment to prescribing polypill in the future.  
42  
43 Compared with free combination medications, FDC therapy has the potential to be relatively  
44  
45 inexpensive due to cheaper drug costs and reduced monitoring<sup>34</sup>, and there is increasing  
46  
47 evidence in the literature supporting the cost-effectiveness of a polypill strategy<sup>35-36</sup>. With  
48  
49 modest costs considered a cornerstone of combination therapy<sup>37</sup>, undertaking cost-effective  
50  
51 evaluations to determine the feasibility of using polypills is urgently needed.  
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54

55  
56 Study participants identified improved compliance as a key advantage  
57  
58 and acknowledged a single medication episode was easier to remember. With frequent dosing  
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3 regimens<sup>38</sup> and polypharmacy associated with poor patient compliance to cardiovascular  
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5 medications<sup>39-40</sup>, a polypill approach offering a simplified medication regimen has the  
6  
7 potential to improve adherence in the treatment of cardiovascular disease<sup>41 20</sup>. Our study  
8  
9 corroborates observations from a patient perspective on whether a polypill could improve  
10  
11 adherence, which highlighted concerns around the efficacy of polypill compared with current  
12  
13 medications and the potential for side-effects<sup>20</sup>.

14  
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16  
17 For caregivers, benefits of polypill included simplifying the medication taking process  
18  
19 and ease in organising pill boxes. In a recent study on factors that influenced caregiving and  
20  
21 medication management, participants recognised complex medication needs as an  
22  
23 impediment to care by increasing the demands placed on the caregiver<sup>42</sup>. Caregivers in our  
24  
25 study recognised that the polypill approach was potentially more convenient for the  
26  
27 pharmacy, an observation which has been confirmed in a recent qualitative investigation  
28  
29 exploring pharmacists views towards a cardiovascular polypill<sup>43</sup>.

30  
31  
32  
33 Stroke survivors expressed a reluctance to adopt a future polypill strategy, citing GP  
34  
35 approval as a key factor. This not only supports the view that cardiovascular patients were  
36  
37 inclined to do what their GPs told them<sup>44</sup> but also highlights the key role health professionals  
38  
39 can play in promoting a polypill approach. Exploring the perspectives of those with direct  
40  
41 experience of the polypill can also contribute to the wider acceptability of a polypill strategy  
42  
43 and should be a priority of future research in the field. A recent investigation of the views of  
44  
45 patients and providers who participated in a polypill trial identified similar advantages and  
46  
47 concerns as our own<sup>45</sup> suggesting that polypill perspectives translate to other regions and  
48  
49 health care settings.

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54 With research suggesting that health practitioners often fail to fully explain the  
55  
56 important elements of medication when first prescribing treatment,<sup>46</sup> uptake of polypill may  
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3 depend not only on the health professional prescribing therapy, but also informing and  
4  
5 encouraging acceptance of the approach among stroke survivors and their caregivers.  
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### 8 **Implications for clinical practice**

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11 Results of this investigation confirm acceptability of a polypill for the secondary  
12 prevention of stroke. However, greater efforts to reassure patients and the willingness of GPs  
13 to endorse such treatment is likely to determine acceptability of this approach over the long  
14 term, particularly as inadequate information and difficulties with new medications are  
15 associated with poor adherence<sup>47</sup>. With adherence to medication in stroke survivors known  
16 to be suboptimal<sup>25</sup>, this patient group may be particularly suited to receiving treatment using  
17 fixed-dose combination polypill therapy. Further research on the efficacy of polypill will also  
18 reassure practitioners whose concerns around inflexibility and the suitability of treatment are  
19 likely to influence the decision to prescribe a polypill for stroke patients.  
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### 32 **Conclusion**

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35 A growing body of evidence suggests a fixed-dose combination polypill may have an  
36 important part to play in the prevention of cardiovascular disease. Our findings contribute to  
37 this knowledge base and offer a unique insight into a potentially exciting role for polypill in  
38 the secondary prevention of stroke. The views of stroke survivors, caregivers and GPs  
39 reported here can play an important role in realising this process, however addressing patients  
40 and practitioners concerns and intensifying efforts to increase acceptability of the polypill  
41 approach are needed. Robustly designed randomised controlled trials can contribute to the  
42 successful implementation and uptake of a polypill strategy for the secondary prevention of  
43 stroke.  
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## Competing Interests

None

## Author/s contribution

Jonathan Mant conceived of the study, is the chief investigator on the polypill programme and commented on the final draft of the manuscript. Jonathan Graffy is a co-investigator on the polypill programme, contributed to the data analysis and commented on the manuscript.

Ricky Mullis is a co-investigator on the polypill programme, contributed to developing the study protocol and commented on the manuscript. Stephen Sutton is a co-investigator on the polypill programme, contributed to the data analysis and commented on the manuscript.

James Jamison contributed to developing the study protocol, conducted the interviews and data analysis and prepared the manuscript for submission.

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<b>Gender</b>	Male: n=21 (75%) Female: n=7 (25%)
<b>Age (Mean: 74yrs)</b>	60-69yrs: n=10 (36%) 70-79yrs: n=11 (39%) 80-89yrs: n=7 (25%)
<b>Ethnicity</b>	White: n=27 (97%), South Asian: n=1 (3%)
<b>Stroke classification</b>	Stroke: n=14 (50%) TIA: n=14 (50%)
<b>Time since stroke</b>	6 mths-2 yrs; n=10 (35%) 3-5 yrs: n=8 (29%)

	6-10 yrs: n=5 (18%) >10 yrs: n=5 (18%)
<b>Diabetes status</b>	Yes: n=9 (32%) No: n=19 (68%)
<b>Smoking status</b>	Non-smoker: n=15 (54%) Ex-smoker: n=11 (39%) Smoker: n=2 (7%)
<b>Interview status</b>	Survivor and caregiver: n=14 (50%) Survivor only: n=14 (50%)
<b>Rankin score</b> <b>MrS-9Q(44)</b>	No symptoms: (0) n=6 (21%) No sig. disability: (1) n=4 (14%) Slight disability: (2) n=6 (21%) Moderate disability: (3) n=4 (14%) Mod severe/ severe disability: (4-5) n=8 (29%)

Table 1. Stroke survivor characteristics

# BMJ Open

## Stroke survivors', caregivers' and GPs' attitudes towards a Polypill for the secondary prevention of stroke: A qualitative interview study

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Keywords:	STROKE MEDICINE, PRIMARY CARE, QUALITATIVE RESEARCH

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3 Stroke survivors', caregivers' and GPs' attitudes towards a  
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6 Polypill for the secondary prevention of stroke: A qualitative  
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10 interview study  
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## ABSTRACT

### Objectives

To understand the perspectives of stroke survivors, caregivers and GPs on a polypill approach, consisting of blood pressure and cholesterol lowering therapies, with or without aspirin, for the secondary prevention of stroke.

### Methods

A qualitative interview study was undertaken in five GP surgeries in the East of England. Twenty-eight survivors of stroke/TIA were interviewed, 14 jointly with a caregiver, along with a convenience sample of five GPs, to assess attitudes towards a polypill and its future use. Topic guides explored attitudes to a polypill, factors likely to influence uptake and long-term use, management of polypill medication and factors influencing the decision to prescribe. Data were analysed using a grounded theory approach. Key themes are presented and illustrated with verbatim quotes.

### Results

The analysis identified three key themes: polypill benefits, polypill concerns and polypill lessons for implementation. Stroke/TIA survivors were positive about the polypill concept and considered it acceptable in the secondary prevention of stroke. Benefits of a polypill included convenience resulting in improved adherence and reduced burden of treatment. Caregivers felt that a polypill would improve medication taking practices, and GPs were open to prescribing it to those at increased cardiovascular risk. However, concerns raised included whether a polypill provided equivalent therapeutic benefit, side-effects through combining medications, consequences of nonadherence, lack of flexibility in regulating dosage, disruption to current treatment and suitability to the wider stroke population.



## Conclusion

Participants supported a polypill approach for secondary prevention of stroke, but significant concerns remain. Further research on the efficacy of a polypill is needed to reassure practitioners whose concerns around inflexibility and treatment suitability are likely to influence the decision to prescribe a polypill for secondary prevention of stroke.

Acceptability among survivors, caregivers and GPs is likely to determine the uptake and subsequent use of a polypill in the future.

Key words: Polypill, Stroke, Qualitative research, Semi-structured interview

Abbreviations: FDC: Fixed-dose combination; CVD: Cardiovascular disease.

## Article summary

### Strengths and limitations

- This research adds to an important body of work exploring cardiovascular polypills and is the first study to focus on attitudes to a polypill for secondary prevention of stroke.
- The findings are strengthened by the inclusion of caregivers who have an important role to play in managing the medication of stroke/TIA survivors.
- Conducting a qualitative assessment of individual perspectives allowed an in-depth examination of the subject area.
- Due to the limited sample size findings may not generalise to the wider stroke population or necessarily represent the views of all GPs

- Future research should consider harder to reach groups such as those who need support to manage medication and may benefit most from a polypill approach.

## INTRODUCTION

Stroke is the fourth most common cause of death in the UK, responsible for approximately 40,000 deaths every year<sup>1</sup> and is also a significant cause of acquired adult disability<sup>2</sup>, with about half of all survivors experiencing some degree of physical or cognitive impairment<sup>3</sup> and left dependent on others<sup>4</sup>.

People who have had a stroke or a transient ischaemic attack (TIA; also known as a mini-stroke) are at higher long-term risk and therefore exposed to the increased possibility of having a further event<sup>5-6</sup>. However, this risk can be substantially reduced through the use of preventative medications such as anti-platelet agents<sup>7</sup> or anticoagulants<sup>8</sup>, as well as cholesterol lowering<sup>9 10</sup> and blood pressure (BP) lowering therapies<sup>11</sup>.

Despite evidence-based guidelines, treatment for stroke often falls below recommended standards<sup>12 13</sup>, and significant deficiencies in secondary prevention care have been reported<sup>14</sup>.

The use of multiple medications to treat CVD is often associated with inappropriate medication use (e.g. under-use, or use of non-appropriate medicines), under-prescription and reduced adherence<sup>15</sup>. A polypill consisting of cholesterol lowering and blood pressure lowering therapies, with or without aspirin in a single pill for the treatment of CVD<sup>16</sup> has been proposed.

Wald and Law (2003) introduced the polypill concept and estimated a theoretical 88% reduction in ischaemic heart disease and 80% reduction in stroke, if taken by everyone over 55<sup>17</sup>. Since then a growing body of literature has developed around a polypill, otherwise

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2  
3 known as a fixed-dose combination (FDC) pill, for the prevention of cardiovascular disease<sup>18</sup>  
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5<sup>19</sup>. A series of recently completed trials investigating the role of a fixed-dose combination  
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7 pill on adherence to medication for secondary prevention demonstrated improved adherence  
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9 for the polypill strategy compared with standard care<sup>20-22</sup>. Elsewhere FOCUS found  
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11 improved adherence for patients with myocardial infarction in the polypill group compared to  
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13 the group given the 3 drugs separately<sup>23</sup>.

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17 To date a small number of studies have investigated the perspectives of patients and health  
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19 care professionals towards a theoretical polypill. Although cardiovascular patients considered  
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21 it convenient, they had concerns around the inflexibility of a polypill<sup>24</sup>, however, GPs would  
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23 consider prescribing it to those who needed secondary prevention medication if it was shown  
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25 to be effective.<sup>25-28</sup> With adherence to medication in stroke survivors known to be  
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27 suboptimal<sup>29</sup>, this group may be particularly suited to treatment with an FDC polypill.

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31 The aim of this study was to explore the attitudes and perspectives of stroke/TIA survivors,  
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33 carers and GPs towards a polypill approach for the secondary prevention of stroke, including  
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35 the benefits and consequences of using a polypill, factors likely to influence uptake, the  
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37 caregiver role in managing medication and GPs' views and attitudes towards prescribing a  
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39 polypill in the future.  
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## 52 **METHODS**

### 53 **Study Design and Participants**

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3 A qualitative study using semi-structured interviews was undertaken. The stroke registers of  
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5 5 GP practices in the East of England were searched. In each practice, a list of prospective  
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7 participants over the age of 55 with a diagnosis of stroke or TIA was generated and screened  
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9 by a GP. Anyone deemed unsuitable for the study was excluded. Purposive sampling was  
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11 used to recruit stroke/TIA survivors with maximum variation characteristics representing a  
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13 spread of socio-economic status<sup>30</sup>, age, gender, and disability<sup>31</sup>. Survivors were sent a study  
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15 information pack and invited to interview. Caregivers were approached through the survivor  
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17 and both were interviewed together, due to time and logistical constraints. All interviews  
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19 were conducted in the stroke survivors' homes. We also sought the views of a convenience  
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21 sample of GPs, each of whom was the study lead for their practice. The GP was contacted by  
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23 phone and an interview arranged at their place of work. The number of interviews conducted  
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25 was determined by data saturation, the point where no new information emerged from  
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27 discussions. Interviews were face to face and consent was taken in person before any  
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29 discussion commenced. Ethical approval was granted by NHS South Yorkshire Research  
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31 Ethics Committee, Ref 13-YH-0067.  
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### 37 **Data Collection**

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40 Data was collected through semi-structured interviews with open ended questions that  
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42 defined the area to be explored<sup>32</sup>. Topic guides were developed by the authors and informed  
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44 by current literature in the field and expertise within the study team which included a GP, a  
45  
46 qualitative researcher and a stroke expert. To ensure ease of understanding and suitability,  
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48 topic guides were piloted with two stroke survivors and checked by a GP. Any appropriate  
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50 recommendations were considered and implemented. Data from the two pilot interviews was  
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52 included in the final analysis. All interviews were conducted by the lead author, JJ, who has  
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54 considerable experience in qualitative research analysis. Field notes were also taken by the  
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56 interviewer. Topics discussed were perceived benefits and consequences of a polypill, factors  
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3 influencing polypill uptake, caregiver views and GPs' beliefs and attitudes towards  
4 prescribing a polypill. The schedule of questions was refined and finalised after the fifth  
5 interview to include questions on the wider experience of stroke as well as understanding of  
6 the polypill approach and the GP relationship. Interviews were audiotaped, lasted 1- 1.5 hours  
7 and were transcribed verbatim.  
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### 13 **Data analysis**

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15 We followed the Strauss and Corbin Grounded Theory approach using constant  
16 comparative analysis<sup>33</sup>. This method permits key points to emerge from the data and to then  
17 be coded individually. A set of codes, representing initial themes, were developed from  
18 chunks of data. Codes were then further refined, and those representing similar concepts were  
19 grouped together to form categories. The identification and refinement of categories  
20 continued until the final themes emerged. Nvivo 9 (QSR Intl, Melbourne, Victoria, Australia)  
21 was used to organise, code and manage the data. Transcripts were entered into the program  
22 and coded by JJ, with 20% double coded independently by SS. Queries arising from coded  
23 transcripts were settled through discussion. Communication with a third author (JG) enabled  
24 clarification and refinement of categories until a consensus was reached.  
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## 61 **RESULTS**

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3 A total of twenty-eight stroke/TIA survivors participated. Fourteen were interviewed alone  
4 and 14 with the caregiver present, who was either a spouse (n=12) or family member (n=2).  
5  
6  
7 Characteristics of survivors are displayed in Table 1 below. Three male GPs and two female  
8  
9  
10 GPs were also interviewed. One GP was white British, one was Chinese and three were of  
11  
12 south Asian origin. Key themes identified reflected the positive and negative aspects of the  
13  
14 polypill approach as well as future use. Sub-themes highlighted benefits and concerns  
15  
16 associated with a polypill approach and factors likely to influence stroke survivors using a  
17  
18 polypill.  
19

20  
21  
22  
23 Table 1 here.  
24  
25  
26

### 27 **Polypill benefits**

28  
29 The concept of a polypill was broadly acceptable to survivors and caregivers. Greater  
30  
31 convenience leading to better adherence, confidence that a polypill was providing the  
32  
33 appropriate treatment, reduced treatment burden, ease of use, and improved medication  
34  
35 management were all considered benefits. For GPs, a polypill facilitated medication taking  
36  
37 and provided flexibility in treatment and convenience around prescribing practices.  
38  
39

40  
41 Convenience

42  
43  
44 Survivors were enthusiastic about one tablet combining all stroke medication and reducing  
45  
46 treatment burden through minimising the inconvenience of managing multiple medications.  
47  
48

49  
50  
51 That is the best thing I've read when it said you might have to take one pill to cover  
52  
53 the lot. Super, because that is just a bugbear, it's a bugbear in life. (pp 11, Male,  
54  
55 73yrs).  
56  
57  
58  
59  
60

1  
2  
3 A single tablet was considered easier to remember and likely to improve overall medication  
4  
5 taking behaviour.  
6  
7

8  
9  
10 I think it's brilliant because erm I, I've got more chance of remembering to take one  
11  
12 tablet than I have of remembering two different times of the day if you like. (pp10,  
13  
14 Male, 66 yrs)  
15  
16

17  
18 Caregivers also endorsed the view that a polypill improved compliance and that it ensured the  
19  
20 appropriate medications were being taken.  
21  
22

23  
24 It means that if you've taken that one you've taken them all. Whereas sometimes if  
25  
26 you run short, you think oh I'll just take that one and forget about the other one until  
27  
28 you go to the doctors and get the refill (pp02, Female, carer).  
29  
30

31  
32 GPs also felt that a polypill had the potential to improve medication adherence.  
33

34  
35 I think that would reduce the pill burden to our patients and I think that's very good  
36  
37 idea... I think he would be very compliant with it, because he is thinking that he is  
38  
39 going to be taking 1 tablet and not 5 tablets....(GP 02, Female).  
40  
41

42  
43 The potential for 'cross-over' treatment in individuals with multiple existing cardiovascular  
44  
45 co-morbidities was mentioned.  
46

47  
48 If you're giving polypill in the form of one pill, even with people with comorbidities  
49  
50 (you're) maybe reducing their number...and might improve overall compliance and it  
51  
52 may have the side effect of improving their comorbidity as well (GP 05, Male).  
53  
54

55  
56 Carers agreed that a polypill made the medication taking process less demanding.  
57  
58  
59  
60

1  
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3  
4  
5 It's logic to me and I think it's an excellent idea if it could be done, certainly instead  
6 of [patient] fiddling about in a saucer trying to pick up tablets.. (pp28, Male, carer).  
7  
8  
9

10  
11  
12 They also felt that the process of obtaining and managing medication was better compared  
13 with using multiple medications.  
14  
15

16  
17  
18 One tablet is good really isn't it, because it means that you if you've taken that one  
19 you've taken them all. Whereas sometimes if you run short, you think oh I'll just take  
20 that and forget about the other one until you go the doctors and get the refill. (pp02,  
21 Female, Carer)  
22  
23  
24  
25  
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27

28  
29  
30 Benefits of correct treatment

31  
32 A polypill offered the benefit of correct medication and it ensured that the patient received  
33 their recommended medications.  
34  
35

36 It could protect, once you had polypills that contained a mixture of medications  
37 which are known not to have...contradictory side-effects...then you would feel very  
38 safe. (pp03, Male, 86 yrs)  
39  
40  
41  
42  
43

44  
45 There was also confidence that components were safe, tested and therefore provided the most  
46 appropriate treatment.  
47  
48  
49

50  
51  
52 I'm all for these things....it might not be good for you, It might not, I don't know I  
53 can't see how because if they're now gonna put four different pills into one they  
54  
55  
56  
57  
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60



1  
2  
3 musta investigated a, b, c and d to put them in one so therefore it's going to be  
4  
5 beneficial to me and anybody else that wants those four in one (pp11, Male, 73yrs).  
6  
7  
8  
9  
10

### 11 **Polypill concerns**

12  
13  
14 Survivors' and caregivers' concerns included polypill noncompliance resulting in missing all  
15  
16 medications, inability to adjust dosage, whether a polypill could maintain the benefits of the  
17  
18 survivors' current secondary prevention medication, timing of a polypill, identifying the  
19  
20 source of polypill side effects and modifying treatment if a component was no longer  
21  
22 required. GPs questioned whether a single pill could treat the entire stroke population, the  
23  
24 cost implications of treatment and the wisdom in modifying a patient's stable treatment  
25  
26 regimen.  
27  
28  
29

#### 30 31 32 **Appropriateness of treatment**

33  
34 Several survivors expressed concern that a polypill may not sustain equivalent therapeutic  
35  
36 benefit of secondary prevention treatment.  
37  
38  
39

40  
41 As far as I'm concerned you've got one tablet with all the ingredients of the  
42  
43 others... if I've got the same erm dosage of statin and if it didn't disturb my  
44  
45 readings then yeah I mean erm what are the objections to it? (pp05, Male, 64 yrs)  
46  
47  
48

49  
50 Several survivors had concerns about the prospect of a 'pill for all', inability to alter dosage  
51  
52 and being less amenable to dose titration, if that was required..  
53  
54  
55  
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2  
3 Would the polypill be in different strengths because like for blood pressure at the  
4 moment I'm taking...12 and a half, and then me cl- clopidogrel is 75..., maybe six  
5  
6 months down the line my blood pressure can reduce, what would that do with the  
7  
8 polypill? (pp21, Female, 68 yrs)  
9  
10

11  
12  
13  
14 Survivors accustomed to scheduled medication regimens also questioned how drugs could  
15  
16 now be combined and taken at a single time point.  
17

18 if you've got them altogether and you're supposed to take those tablets at different  
19  
20 times of the day, how's it going to work? Is it going to upset your system? (pp22,  
21  
22 Female, 71 yrs).  
23  
24

25  
26  
27 Suitability of the polypill strategy  
28

29 Survivors questioned the ease of managing treatment if one or more components were no  
30  
31 longer required.  
32

33  
34 Would it only be suitable for somebody who's taking four of that particular  
35  
36 medication? But what would happen if say the Dr said, you're not so bad so you  
37  
38 don't need to take that particular tablet? (pp16, Female, 82 yrs)  
39  
40

41  
42  
43 A few expressed concerns around the inclusion of statins in any combination pill.  
44

45  
46  
47 Yes has that got anything to do with statins? I've read a lot about statins and I'm  
48  
49 afraid I feel I wouldn't want to take them. Because the side effects and everything.  
50  
51 (pp19, Female, carer)  
52  
53  
54  
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1  
2  
3 GPs were cautious, suggesting a polypill could be better suited to those on similar  
4  
5 medications whose treatment was well-established.  
6  
7  
8

9  
10 I think the right drugs in the right combinations there, it, would potentially be helpful  
11  
12 for a cohort of people. I don't think it will be for everyone but there will be a cohort  
13  
14 of people who will probably be on very similar drugs... (GP03, Male)  
15  
16

17  
18 Survivors and carers were also concerned that poor adherence would lead to missing all their  
19  
20 secondary prevention drugs.  
21  
22

23 If you're gonna give them a polypill that is three or four tablets and they don't bother  
24  
25 taking that..They're gonna be worse off (pp14, Male, Carer)  
26  
27

28  
29 Given the unique needs of stroke survivors, some suggested that multiple polypills may be  
30  
31 needed.  
32  
33

34  
35  
36 They don't give me three separate ones for no reason, there must be a reason for it.  
37  
38 You can't do that with a polypill unless you have a hundred polypills all different  
39  
40 medications and different combinations (pp18, Male, 88 yrs).  
41  
42  
43  
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#### 49 Polypill side effects

50  
51 The likelihood of polypill side effects led many to question the suitability of single pill  
52  
53 treatment.  
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1  
2  
3 The fine tuning takes a bit of doing so w- with the one pill I got my bit of a doubt that  
4  
5 it might work for some people but it might not work for everybody you see (pp04,  
6  
7 Male, 80 yrs).  
8  
9

10  
11  
12 For GPs, a further problem resulting from this was the potential difficulty in identifying the  
13  
14 component of a polypill responsible for side effects.  
15

16  
17  
18 My personal anxiety is about side effects when you club two, three medicines  
19  
20 together, if one of them, one of the components is, is causing the side effect then  
21  
22 you'll not know, you may have to again change.. (GP 05, Male)  
23  
24  
25

#### 26 27 Medication adjustment

28  
29 GPs questioned the benefit in altering established medication routines to accommodate a  
30  
31 polypill in those who were already taking their medication as directed.  
32  
33

34  
35 If you've got, as I said, a very motivated patient they are happy with what they are  
36  
37 taking, then we don't probably have to intervene, but we may have to give to people  
38  
39 who are not that motivated or compliant. (GP 05, Male)  
40  
41

42  
43 They also expressed concern about the inconvenience of having to re-adjust future treatment  
44  
45 if polypill components were no longer required.  
46  
47

48  
49 If somebody has a problem ok well we'll just stop using the polypill and give them  
50  
51 the individual ones but with that stopping and chopping and changing people will say  
52  
53 they've changed my tablets again, that becomes an issue. (GP 04, Male)  
54  
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1  
2  
3 However, inflexibility of a polypill and the inability to manipulate dosage was perhaps the  
4  
5 greatest concern among GPs.  
6

7 We do switch around quite a bit different brands, different sizes, statins and  
8  
9 sometimes it may not be the right dose but you kind of slowly edge it in... It would  
10  
11 be advantageous if it was a single pill but that would be maybe a bit difficult with  
12  
13 polypill...It's the fine tuning that's difficult..(GP 01, Female)  
14  
15  
16  
17

18 Caregivers also expressed concern around the inflexibility of a polypill and the potential  
19  
20 difficulties in adjusting dosage.  
21

22 You would have to get the right strengths of each tablet. "Where you were on atenolol  
23  
24 50 you are now on 25". Sometimes they change the strength of the tablet. That's  
25  
26 where it would be harder to change with the polypill (pp25, Female, carer)  
27  
28  
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30  
31  
32

### 33 34 Size of polypill

35  
36 GPs raised concerns that a large pill could actually discourage medication taking.  
37

38 Yeah is it a horse tablet? ...that's going to have the other, the opposite effect on  
39  
40 compliance that we want... People are going to start breaking it having half now and  
41  
42 half twelve hours later..(GP 04, Male).  
43  
44  
45  
46

### 47 48 Cost of polypill

49  
50 The burden of the polypill on NHS resources was also raised with a number of GPs  
51  
52 suggesting that a more expensive pill could be difficult to prescribe.  
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3 If it is cheaper then there won't be an issue at all. if it comes out to be more  
4  
5 expensive than the four tablets which you are giving individually to the patient  
6  
7 then it comes to be an issue (GP 02, Female)  
8  
9

10  
11  
12 Cost implications for practices and pharmacies dispensing a polypill were also considered  
13  
14 with GPs acknowledging the likelihood of reduced revenues associated with a single pill.  
15

16  
17  
18 They get an item fee for each thing they prescribe so if you have 4 drugs you get a  
19  
20 fee for each, if you put it in 1 pill that will account for one (GP 04, Male)  
21  
22  
23  
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25  
26

### 27 **Polypill lessons for implementation**

28  
29 Survivors thought that whether they used a polypill in the future would depend on their  
30  
31 doctor's recommendation, but they also questioned the need for a polypill given their  
32  
33 satisfaction with current treatment. GPs acknowledged that their support was likely to be  
34  
35 influential in the decision to use a polypill and believed the approach should be adopted if it  
36  
37 was found to be beneficial to the patient. While stroke/ TIA survivors were generally positive  
38  
39 about the polypill approach, many were non-committal on its future use, largely due to the  
40  
41 lack of existing evidence.  
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#### 52 **Polypill recommendation**

53  
54 Many survivors felt that whether they used a polypill in the future was likely to depend on  
55  
56 their doctor recommending the treatment.  
57  
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3 It sounds good but w- we've got to, we would have to weigh up, listen to what the  
4 doctors say and the consultants and see what history, because this polypill, from  
5 what we've hear. Very, very little, it's quite new, that's all we know. (pp22, Male,  
6 carer)  
7  
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9  
10

11  
12  
13  
14 Satisfied with current medication  
15

16  
17  
18 Being content with their current medication also made survivors less enthusiastic about  
19 taking a polypill which may have unwanted side-effects.  
20  
21  
22  
23

24  
25 Why take a tablet that perhaps will affect you. Plus the fact I'm perfectly happy with  
26 what I'm on, you know, at the moment anyway (pp01, Female, 71 yrs).  
27  
28  
29  
30

31  
32 Endorsement of the polypill  
33

34 GPs agreed that if they endorsed polypill, stroke/TIA survivors were likely to accept it as a  
35 treatment for secondary stroke and commit to using it in the future.  
36  
37  
38  
39

40 I think the majority of our current patients if we told them we think this is the right  
41 thing to do would probably be happy with that. It's a fairly easy argument (GP 03,  
42 Male).  
43  
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49 Furthermore, there was an obligation to try new and innovative treatments like the polypill, if  
50 its potential benefits were proven.  
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2  
3 I welcome change and innovation I'm excited by it... you don't know until you've  
4  
5 tried it... We have to try it if there was a potential benefit there for people (GP04,  
6  
7 Male)  
8  
9

## 10 DISCUSSION

### 11 Summary of main findings

12  
13 Stroke/TIA survivors and caregivers were positive about the polypill concept which they saw  
14  
15 as offering greater convenience, reducing the burden of treatment and improving adherence.  
16  
17 A polypill would also ensure that patients received the correct treatment and that medications  
18  
19 were safe. There were concerns among survivors around the suitability of a polypill if not  
20  
21 already using the components or if one component was no longer needed. Other limitations  
22  
23 included the potential for side-effects and the inflexibility of a single pill approach. GPs felt  
24  
25 that a more expensive pill would be problematic and acknowledged that their endorsement  
26  
27 was key to it being accepted. For survivors, the decision to use a polypill would depend on  
28  
29 the GP's recommendation, but those who were satisfied with their current treatment regimen  
30  
31 felt less inclined to change to a polypill.  
32  
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### 42 Strengths and Limitations

43  
44 A strength of this study is that it adds to a growing and important body of research on  
45  
46 attitudes towards a cardiovascular polypill with a focus on secondary prevention of stroke.  
47  
48 Second, the use of semi-structured interviews enabled an in-depth assessment of individual  
49  
50 perspectives. A further strength is the inclusion of caregivers, who can make a significant  
51  
52 contribution in the future management of polypill treatment. We believe that being  
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2  
3 interviewed by a qualitative researcher rather than a health care professional encouraged  
4  
5 survivors' to be open and to engage in discussion.  
6  
7

8  
9 However, limitations include a relatively small sample of GPs' recruited from five general  
10 practice surgeries. Although every effort was made to recruit a representative sample with  
11 varied disability, most survivors who responded to our request to participate were primarily  
12 able bodied with no significant stroke symptoms and independently managed their own  
13 medication. In addition, survivors were almost exclusively White British. With some ethnic  
14 groups, particularly south Asians, known to be at considerably higher risk of cardiovascular  
15 disease<sup>34</sup>, the study may have benefited from the including individuals who are considered to  
16 be at a greater risk from stroke and likely to be prospective users of polypill therapy. As a  
17 result, survivors in our study may not represent the wider stroke population. Furthermore,  
18 only five GPs were interviewed, and their opinions may not reflect those of the GP  
19 population at large. With all caregivers interviewed in the presence of a survivor, this may  
20 have contributed to individuals responding in a socially desirable manner and understating  
21 their true views on secondary prevention and the polypill. Investigating a polypill among  
22 survivors with significant symptoms and dependent on others to organise their tablets may be  
23 an area for future research in the field. Finally, future research should aim to include those  
24 harder to reach groups of survivors who may benefit most from a polypill approach.  
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#### 44 **Comparisons with existing literature**

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46  
47 The inflexibility of treatment and the potential for side-effects were considered key  
48 challenges of a polypill approach. Concerns about side-effects have previously been  
49 identified as influencing medication taking behaviour<sup>35</sup> and recognised as a significant  
50 barrier to adherence in cardiovascular disease medication<sup>36</sup>. Our findings are also in line with  
51 a recent UK primary care investigation in which patients considered a secondary prevention  
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2  
3 polypill acceptable, but were concerned about components interacting and inflexibility of  
4  
5 treatment<sup>37</sup>. The inability to adapt polypill dosage and the suitability of fixed dose treatment  
6  
7 was a key concern for GPs in our study and has been previously reported in studies exploring  
8  
9 polypill attitudes among GPs elsewhere. A small survey of 17 practitioners in New Zealand  
10  
11 reported that having no choice of polypill components or doses was the thing GPs disliked  
12  
13 most about the concept of a polypill<sup>25</sup>. In another UK study of primary healthcare  
14  
15 professionals, inability to titrate dosage was considered a major disadvantage of the polypill  
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The GPs in our study agreed that cost was a potential impediment to prescribing a polypill in the future. Compared with free combination medications, FDC therapy has the potential to be relatively inexpensive due to cheaper drug costs and reduced monitoring<sup>38</sup>, and there is increasing evidence in the literature supporting the cost-effectiveness of a polypill strategy<sup>39-40</sup>. With modest costs considered a cornerstone of combination therapy<sup>41</sup>, evaluations of the cost-effectiveness of using polypills is urgently needed.

Improved adherence was recognised as a key advantage of a polypill, and survivors acknowledged that a single medication episode was easier to remember. With frequent dosing regimens<sup>42</sup> and polypharmacy associated with poor patient compliance to cardiovascular medications<sup>43,44</sup>, a polypill approach offering a simplified medication regimen has the potential to improve adherence in the treatment of cardiovascular disease<sup>45,24</sup>. Our study corroborates observations from a patient perspective on whether a polypill could improve adherence, which highlighted concerns around the efficacy of a polypill compared with current medications and the potential for side-effects<sup>24</sup>.

For caregivers, benefits of a polypill included simplifying the medication taking process and ease in organising pill boxes. In a recent study on factors that influenced

1  
2  
3 caregiving and medication management, participants recognised complex medication needs  
4  
5 as an impediment to care by increasing the demands placed on the caregiver <sup>46</sup>. Caregivers in  
6  
7 our study recognised that a polypill approach was potentially more convenient for the  
8  
9 pharmacy, an observation which has been confirmed in a recent qualitative investigation  
10  
11 exploring pharmacists' views towards a cardiovascular polypill <sup>47</sup>.  
12  
13

14  
15 Stroke/TIA survivors expressed a reluctance to adopt a future polypill strategy, citing  
16  
17 GP approval as a key factor. This not only supports the view that cardiovascular patients were  
18  
19 inclined to do what their GPs told them <sup>48</sup> but also highlights the key role GPs can play in  
20  
21 promoting a polypill approach. Exploring the perspectives of those with direct experience of  
22  
23 the polypill can contribute to the wider acceptability of a polypill strategy and should  
24  
25 continue to be a priority of future research. While a polypill was acceptable to most patients  
26  
27 of the UMPIRE trial, some felt that fixed-dose combination therapy was less tailored to  
28  
29 individual patient needs <sup>49</sup>. A recent investigation of the views of cardiovascular patients and  
30  
31 providers who participated in polypill trials reported similar advantages and concerns to those  
32  
33 identified in our study <sup>50</sup>, suggesting that polypill perspectives translate to other regions and  
34  
35 health care settings.  
36  
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39  
40 With research suggesting that health practitioners often fail to fully explain the  
41  
42 important elements of medication when first prescribing treatment, <sup>51</sup> uptake of a polypill  
43  
44 may depend not only on the GP prescribing therapy but also on informing and encouraging  
45  
46 acceptance of the approach among stroke/TIA survivors and their caregivers.  
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## 55 56 **Implications for clinical practice** 57 58 59 60

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3 Our findings suggest that survivors, caregivers and GPs were positive about a polypill  
4 but also had concerns around this approach for stroke prevention. Greater efforts are needed  
5 to reassure survivors and caregivers while GPs' willingness to endorse a polypill may  
6 determine long-term acceptability of this approach, particularly as inadequate information  
7 and difficulties with new medications are associated with poor adherence<sup>52</sup>. Further studies  
8 are also needed with a broader sample of GPs to corroborate the findings reported. With  
9 adherence among stroke survivors known to be suboptimal<sup>29</sup>, this patient group may be  
10 particularly suited to receiving treatment using fixed-dose combination polypill therapy.  
11 Further research on the efficacy of a polypill will also reassure practitioners whose concerns  
12 around inflexibility and the suitability of treatment are likely to influence the decision to  
13 prescribe a polypill to stroke/TIA survivors.  
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## 28 **Conclusion**

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31 A growing body of evidence suggests that a fixed-dose combination polypill may  
32 have a role in the prevention of cardiovascular disease. Our findings contribute to the  
33 growing literature on cardiovascular polypills, offer a unique insight around stroke and may  
34 inform future research and clinical practice in the area of secondary stroke prevention in the  
35 UK. A polypill may also have a role to play in improving adherence among stroke survivors.  
36 The findings have informed the development of PROPS - Preventative Role of a fixed dose  
37 combination Pill in Stroke -, a multi-centre open label randomised controlled trial of a fixed  
38 dose combination pill versus standard care for secondary prevention of stroke in a primary  
39 care setting. (EudraCT number: 201300472229). However, addressing patients' and  
40 practitioners' concerns and intensifying efforts to increase the acceptability of this treatment  
41 approach is likely to determine future use of a cardiovascular polypill for the secondary  
42 prevention of stroke.  
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Data sharing statement: No additional data available.

Competing Interests: None.

Author/s contribution: Jonathan Mant conceived the study, is the chief investigator on the polypill programme and commented on the final draft of the manuscript. Jonathan Graffy is a co-investigator on the polypill programme, contributed to the data analysis and commented on the manuscript. Ricky Mullis is a co-investigator on the polypill programme, contributed to developing the study protocol and commented on the manuscript. Stephen Sutton is a co-investigator on the polypill programme, contributed to the data analysis and commented on the manuscript. James Jamison contributed to developing the study protocol, conducted the interviews and data analysis and prepared the manuscript for submission.

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<b>Gender</b>	Male: n=21 (75%) Female: n=7 (25%)
<b>Age (Mean: 74yrs)</b>	60-69yrs: n=10 (36%) 70-79yrs: n=11 (39%) 80-89yrs: n=7 (25%)
<b>Ethnicity</b>	White: n=27 (97%), South Asian: n=1 (3%)
<b>Stroke classification</b>	Stroke: n=14 (50%) TIA: n=14 (50%)
<b>Time since stroke</b>	6 mths-2 yrs: n=10 (35%) 3-5 yrs: n=8 (29%) 6-10 yrs: n=5 (18%) >10 yrs: n=5 (18%)
<b>Diabetes status</b>	Yes: n=9 (32%) No: n=19 (68%)
<b>Smoking status</b>	Non-smoker: n=15 (54%) Ex-smoker: n=11 (39%) Smoker: n=2 (7%)
<b>Interview status</b>	Survivor and caregiver: n=14 (50%) Survivor only: n=14 (50%)
<b>Rankin score*</b>	No symptoms: (0) n=6 (21%)
<b>MrS-9Q</b>	No sig. disability: (1) n=4 (14%) Slight disability: (2) n=6 (21%)

	Moderate disability: (3) n=4 (14%)
	Mod severe/ severe disability: (4-5) n=8 (29%)

Table 1. Stroke survivor characteristics. \*Rankin score is derived from a scale that measures the degree of disability in the daily activities of people who may have suffered a stroke

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## Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No	Item	Guide questions/description	
<b>Domain 1: Research team and reflexivity</b>			
Personal Characteristics			
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group?	JJ was the interviewer
2.	Credentials	What were the researcher's credentials? <i>E.g. PhD, MD</i>	BSc, MSc
3.	Occupation	What was their occupation at the time of the study?	Research Assistant/ PhD Student
4.	Gender	Was the researcher male or female?	Male
5.	Experience and training	What experience or training did the researcher have?	JJ is a researcher with experience in undertaking qualitative research.
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement?	No
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? <i>e.g. personal goals, reasons for doing the research</i>	Participants were informed that the researcher was a PhD student who worked for the University of Cambridge
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? <i>e.g. Bias, assumptions, reasons and interests in the research topic</i>	Participants know that the researcher works in a primary care unit and is investigating as new approach to secondary stroke prevention using a Polypill
<b>Domain 2: study design</b>			
Theoretical framework			
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? <i>e.g. grounded theory, discourse analysis, ethnography, phenomenology, content</i>	Grounded Theory

No	Item	Guide questions/description	
		<i>analysis</i>	
Participant selection			
10.	Sampling	How were participants selected? <i>e.g. purposive, convenience, consecutive, snowball</i>	Purposive/ convenience sampling –stroke survivors were selected purposively in order to achieve a range of gender, socio economic status, stroke severity. Caregivers and GPs were a convenience sample recruited through the survivors and as the GP leading the study within the practice, respectively.
11.	Method of approach	How were participants approached? <i>e.g. face-to-face, telephone, mail, email</i>	Stroke survivors were approached by letter. Carers were approached directly through the stroke survivor. GPs were approached by phone.
12.	Sample size	How many participants were in the study?	28 stroke survivors, 14 caregivers, 5 GPs
13.	Non-participation	How many people refused to participate or dropped out? Reasons?	No one refused to participate
Setting			
14.	Setting of data collection	Where was the data collected? <i>e.g. home, clinic, workplace</i>	Data was collected in the patients/caregivers home and in the GPs place of work
15.	Presence of non-participants	Was anyone else present besides the participants and researchers?	Other than the caregiver who participated in joint interviews, no-one else was present during the interview..
16.	Description of sample	What are the important characteristics of the sample? <i>e.g. demographic data, date</i>	Gender, stroke status, age
Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Yes. An interview guide was developed for survivors, caregivers and GPs. Guides were tested by 2 stroke survivors and a clinical researcher commented on the GP guide.
18.	Repeat interviews	Were repeat interviews carried out? If yes, how	No

No	Item	Guide questions/description	
		many?	
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?	Yes. All interviews were audio recorded.
20.	Field notes	Were field notes made during and/or after the interview or focus group?	Yes. Field notes were taken during interviews.
21.	Duration	What was the duration of the interviews or focus group?	Interviews lasted between 1 and 1.5 hours
22.	Data saturation	Was data saturation discussed?	Yes
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction?	No
<b>Domain 3: analysis and findings</b>			
Data analysis			
24.	Number of data coders	How many data coders coded the data?	2 authors contributed to the coding process. JJ coded all of the interviews. 20% were also coded independently by SS.
25.	Description of the coding tree	Did authors provide a description of the coding tree?	Not explicitly
26.	Derivation of themes	Were themes identified in advance or derived from the data?	Themes were generated from the data
27.	Software	What software, if applicable, was used to manage the data?	Nvivo 9
28.	Participant checking	Did participants provide feedback on the findings?	No.
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. <i>participant number</i>	Yes, quotations were presented in the text to illustrate the themes.. Participants were identified by a number.
30.	Data and findings consistent	Was there consistency between the data presented and the findings?	Yes
31.	Clarity of major	Were major themes clearly	Yes



No	Item	Guide questions/description	
	themes	presented in the findings?	
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Yes. Both key themes and sub-themes are reported. Restrictions on word count prevented themes being discussed extensively

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# BMJ Open

## Stroke survivors', caregivers' and GPs' attitudes towards a Polypill for the secondary prevention of stroke: A qualitative interview study

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Complete List of Authors:	JAMISON, JAMES; UNIVERSITY OF CAMBRIDGE, PUBLIC HEALTH & PRIMARY CARE GRAFFY, JONATHAN; UNIVERSITY OF CAMBRIDGE, PUBLIC HEALTH & PRIMARY CARE Mullis, Ricky; University of Cambridge, General Practice & Primary Care Research Centre Mant, Jonathan; University of Cambridge, General Practice and Primary Care Research Unit Sutton, Stephen; University of Cambridge,
<b>Primary Subject Heading</b>:	Cardiovascular medicine
Secondary Subject Heading:	Qualitative research
Keywords:	STROKE MEDICINE, PRIMARY CARE, QUALITATIVE RESEARCH

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Manuscripts

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3 Stroke survivors', caregivers' and GPs' attitudes towards a  
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6 Polypill for the secondary prevention of stroke: A qualitative  
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10 interview study  
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16 \*James Jamison<sup>1</sup>, MSc

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## ABSTRACT

### Objectives

To understand the perspectives of stroke survivors, caregivers and GPs on a polypill approach, consisting of blood pressure and cholesterol lowering therapies, with or without aspirin, for the secondary prevention of stroke.

### Methods

A qualitative interview study was undertaken in five GP surgeries in the East of England. Twenty-eight survivors of stroke/TIA were interviewed, fourteen of them with a caregiver present, along with a convenience sample of five GPs, to assess attitudes towards a polypill and future use. Topic guides explored participants attitudes, potential uptake and long-term use, management of polypill medication and factors influencing the decision to prescribe. Data were analysed using a grounded theory approach. Key themes are presented and illustrated with verbatim quotes.

### Results

The analysis identified three key themes: polypill benefits, polypill concerns and polypill lessons for implementation. Stroke/TIA survivors were positive about the polypill concept and considered it acceptable in the secondary prevention of stroke. Perceived benefits of a polypill included convenience resulting in improved adherence and reduced burden of treatment. Caregivers felt that a polypill would improve medication taking practices, and GPs were open to prescribing it to those at increased cardiovascular risk. However, concerns raised included whether a polypill provided equivalent therapeutic benefit, side-effects through combining medications, consequences of nonadherence, lack of flexibility in

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3 regulating dosage, disruption to current treatment and suitability to the wider stroke  
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5 population.  
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## 9 Conclusion

10 Participants acknowledged potential advantages in a polypill approach for secondary  
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12 prevention of stroke, however, significant concerns remain. Further research on the efficacy  
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14 of a polypill is needed to reassure practitioners whose concerns around inflexibility and  
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16 treatment suitability are likely to influence the decision to prescribe a polypill for secondary  
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18 prevention of stroke. Acceptability among survivors, caregivers and GPs is likely to  
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20 determine the uptake and subsequent use of a polypill in the future.  
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27 Key words: Polypill, Stroke, Qualitative research, Semi-structured interview  
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33 Abbreviations: FDC: Fixed-dose combination; CVD: Cardiovascular disease.  
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## 40 Article summary

### 41 Strengths and limitations

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- 46 • This research adds to an important body of work exploring cardiovascular polypills  
47 and is the first study to focus on attitudes to a polypill for secondary prevention of  
48 stroke.  
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  - 50 • The findings are strengthened by the inclusion of caregivers who have an important  
51 role to play in managing the medication of stroke/TIA survivors.  
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- Conducting a qualitative assessment of individual perspectives allowed an in-depth examination of the subject area.
- Due to the limited sample size findings may not generalise to the wider stroke population or necessarily represent the views of all GPs
- Future research should consider harder to reach groups such as those who need support to manage medication and may benefit most from a polypill approach.

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Data sharing statement: No additional data available.

## INTRODUCTION

Stroke is the fourth most common cause of death in the UK, responsible for approximately 40,000 deaths every year<sup>1</sup> and is also a significant cause of acquired adult disability<sup>2</sup>, with about half of all survivors experiencing some degree of physical or cognitive impairment<sup>3</sup> and left dependent on others<sup>4</sup>.

People who have had a stroke or a transient ischaemic attack (TIA; also known as a mini-stroke) are at higher long-term risk and therefore exposed to the increased possibility of having a further event<sup>5-6</sup>. However, this risk can be substantially reduced through the use of preventative medications such as anti-platelet agents<sup>7</sup> or anticoagulants<sup>8</sup>, as well as cholesterol lowering<sup>9 10</sup> and blood pressure (BP) lowering therapies<sup>11</sup>.

Despite evidence-based guidelines, treatment for stroke often falls below recommended standards<sup>12 13</sup>, and significant deficiencies in secondary prevention care have been reported<sup>14</sup>.

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3 The use of multiple medications to treat CVD is often associated with inappropriate  
4 medication use (e.g. under-use, or use of non-appropriate medicines), under-prescription and  
5 reduced adherence <sup>15</sup>. A polypill consisting of cholesterol lowering and blood pressure  
6 lowering therapies, with or without aspirin in a single pill for the treatment of CVD <sup>16</sup> has  
7 been proposed.  
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11 Wald and Law (2003) introduced the polypill concept and estimated a theoretical 88%  
12 reduction in ischaemic heart disease and 80% reduction in stroke, if taken by everyone over  
13 55 <sup>17</sup>. Since then a growing body of literature has developed around a polypill, otherwise  
14 known as a fixed-dose combination (FDC) pill, for the prevention of cardiovascular disease <sup>18</sup>  
15 <sup>19</sup>. A series of recently completed trials investigating the role of a fixed-dose combination  
16 pill on adherence to medication for secondary prevention demonstrated improved adherence  
17 for the polypill strategy compared with standard care <sup>20-22</sup>. Elsewhere FOCUS found  
18 improved adherence for patients with myocardial infarction in the polypill group compared to  
19 the group given the 3 drugs separately<sup>23</sup>.  
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35 To date a small number of studies have investigated the perspectives of patients and health  
36 care professionals towards a theoretical polypill. Although cardiovascular patients considered  
37 it convenient, they had concerns around the inflexibility of a polypill <sup>24</sup>, however, GPs would  
38 consider prescribing it to those who needed secondary prevention medication if it was shown  
39 to be effective. <sup>25-28</sup> With adherence to medication in stroke survivors known to be  
40 suboptimal <sup>29</sup>, this group may be particularly suited to treatment with an FDC polypill.  
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50 The aim of this study was to explore the attitudes and perspectives of stroke/TIA survivors,  
51 carers and GPs towards a polypill approach for the secondary prevention of stroke, including  
52 the benefits and consequences of using a polypill, factors likely to influence uptake, the  
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3 caregiver role in managing medication and GPs' views and attitudes towards prescribing a  
4  
5 polypill in the future.  
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## 10 11 **METHODS**

### 12 13 **Study Design and Participants**

14 A qualitative study using semi-structured interviews was undertaken. The stroke registers of  
15  
16 5 GP practices in the East of England were searched. The criteria for inclusion of stroke  
17  
18 survivors was being over the age of 55, with a diagnosis of stroke or TIA and able to speak  
19  
20 English. Based on these criteria, a list of prospective participants was generated by the  
21  
22 practice administrator. The list was then screened by the practice GP and anyone deemed  
23  
24 unsuitable, such as those unable to provide informed consent or who were terminally or  
25  
26 seriously ill, was removed. Purposive sampling was used to recruit stroke/TIA survivors with  
27  
28 maximum variation characteristics representing a spread of socio-economic status<sup>30</sup>, age,  
29  
30 gender, and disability<sup>31</sup>. Survivors were sent a study information pack and invited to  
31  
32 interview. Caregivers were approached by the stroke survivor with a study information pack  
33  
34 and invited to participate. All caregivers were subsequently interviewed in the presence of a  
35  
36 stroke survivor. Due to time constraints we chose not to interview caregivers separately. All  
37  
38 interviews were conducted in the stroke survivors' homes. We also sought the views of a  
39  
40 convenience sample of GPs, each of whom was the study lead for their practice. The GP was  
41  
42 contacted by phone and an interview arranged at their place of work. The number of  
43  
44 interviews conducted was determined by data saturation, the point where no new information  
45  
46 emerged from discussions. Interviews were face to face and consent was taken in person  
47  
48 before any discussion commenced. Ethical approval was granted by NHS South Yorkshire  
49  
50 Research Ethics Committee, Ref 13-YH-0067.  
51  
52  
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57

### 58 59 **Data Collection**



1  
2  
3 Data was collected through semi-structured interviews with open ended questions that  
4 defined the area to be explored<sup>32</sup>. Topic guides were developed by the authors and informed  
5 by current literature in the field and expertise within the study team which included a GP, a  
6 qualitative researcher and a stroke expert. To ensure ease of understanding and suitability,  
7 topic guides were piloted with two stroke survivors and checked by a GP. Any appropriate  
8 recommendations were considered and implemented. Data from the two pilot interviews was  
9 included in the final analysis. All interviews were conducted by the lead author, JJ, who has  
10 considerable experience in qualitative research analysis. Field notes were also taken by the  
11 interviewer. Topics discussed were perceived benefits and consequences of a polypill, factors  
12 influencing polypill uptake, caregiver views and GPs' beliefs and attitudes towards  
13 prescribing a polypill. See Supplementary file 1 for the interview schedule. The schedule of  
14 questions was refined and finalised after the fifth interview to include questions on the wider  
15 experience of stroke as well as understanding of the polypill approach and the GP  
16 relationship. Interviews were audiotaped, lasted 1- 1.5 hours and were transcribed verbatim.  
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### 35 **Data analysis**

36  
37 We followed the Strauss and Corbin Grounded Theory approach using constant  
38 comparative analysis<sup>33</sup>. This method permits key points to emerge from the data and to then  
39 be coded individually. A set of codes, representing initial themes, were developed from  
40 chunks of data. Codes were then further refined, and those representing similar concepts were  
41 grouped together to form categories. The identification and refinement of categories  
42 continued until the final themes emerged. Nvivo 9 (QSR Intl, Melbourne, Victoria, Australia)  
43 was used to organise, code and manage the data. Transcripts were entered into the program  
44 and coded by JJ, with 20% double coded independently by SS. Queries arising from coded  
45 transcripts were settled through discussion. Communication with a third author (JG) enabled  
46 clarification and refinement of categories until a consensus was reached.  
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## RESULTS

A total of twenty-eight stroke/TIA survivors participated. Fourteen were interviewed alone and 14 with the caregiver present, who was either a spouse (n=12) or family member (n=2). Characteristics of survivors are displayed in Table 1 below. Three male GPs and two female GPs were also interviewed. One GP was white British, one was Chinese and three were of south Asian origin. Key themes identified reflected the positive and negative aspects of the polypill approach as well as future use. Sub-themes highlighted benefits and concerns associated with a polypill approach and factors likely to influence stroke survivors using a polypill.

Table 1 here.

### Polypill benefits

The concept of a polypill was broadly acceptable to survivors and caregivers. Greater convenience leading to better adherence, confidence that a polypill was providing the appropriate treatment, reduced treatment burden, ease of use, and improved medication management were all considered benefits. For GPs, a polypill facilitated medication taking and provided flexibility in treatment and convenience around prescribing practices.

#### Convenience

Survivors were enthusiastic about one tablet combining all stroke medication and reducing treatment burden through minimising the inconvenience of managing multiple medications.

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2  
3  
4  
5 That is the best thing I've read when it said you might have to take one pill to cover  
6  
7 the lot. Super, because that is just a bugbear, it's a bugbear in life. (pp 11, Male,  
8  
9 73yrs).  
10

11  
12  
13  
14 A single tablet was considered easier to remember and likely to improve overall medication  
15  
16 taking behaviour.  
17  
18  
19

20  
21 I think it's brilliant because erm I, I've got more chance of remembering to take one  
22  
23 tablet than I have of remembering two different times of the day if you like. (pp10,  
24  
25 Male, 66 yrs)  
26  
27  
28

29  
30 Caregivers also endorsed the view that a polypill improved compliance and that it ensured the  
31  
32 appropriate medications were being taken.  
33  
34  
35

36  
37 It means that if you've taken that one you've taken them all. Whereas sometimes if  
38  
39 you run short, you think oh I'll just take that one and forget about the other one until  
40  
41 you go to the doctors and get the refill (pp02, Female, carer).  
42  
43  
44

45  
46 GPs also felt that a polypill had the potential to improve medication adherence.  
47  
48

49  
50 I think that would reduce the pill burden to our patients and I think that's very good  
51  
52 idea... I think he would be very compliant with it, because he is thinking that he is  
53  
54 going to be taking 1 tablet and not 5 tablets....(GP 02, Female).  
55  
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3 The potential for 'cross-over' treatment in individuals with multiple existing cardiovascular  
4 co-morbidities was mentioned.  
5  
6

7 If you're giving polypill in the form of one pill, even with people with comorbidities  
8 (you're) maybe reducing their number...and might improve overall compliance and it  
9 may have the side effect of improving their comorbidity as well (GP 05, Male).  
10  
11  
12

13  
14  
15  
16 For carers, the polypill approach made the medication taking process less demanding.  
17  
18

19  
20 It's logic to me and I think it's an excellent idea if it could be done, certainly instead  
21 of [*patient*] fiddling about in a saucer trying to pick up tablets.. (pp28, Male, carer).  
22  
23  
24

25  
26  
27 They also felt that the process of managing medication was better, compared with using  
28 multiple medications.  
29  
30  
31

32  
33  
34 Well if it's only one tablet a day it would be quicker, wouldn't it? for a start. I mean I  
35 usually sit on a night-time and do that (pillbox) when I'm watching telly. There's a  
36 few times I've missed out the odd tablet or put a double in or put too many in so I  
37 mean that would be easier. (pp02, Female, carer)  
38  
39  
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45 Benefits of correct treatment

46  
47 A polypill offered the benefit of correct medication and it ensured that the patient received  
48 their recommended medications.  
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3 It could protect, once you had polypills that contained a mixture of medications  
4 which are known not to have...contradictory side-effects...then you would feel very  
5 safe. (pp03, Male, 86 yrs)  
6  
7  
8  
9

10  
11 And as long as it's whether it's one pill or four pills so you know this is my point of  
12 view I don't think it's going to affect I mean other people might oh yeah I could have  
13 four pills instead of one and they'll start worrying about it but no I erm I just accept  
14 that, that the people are doing their job properly and getting their facts right... as I say  
15 as long as the scientists have got it alright you know you've got to have faith in them  
16 (pp08, Male, 87 yrs)  
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29 There was also confidence that components were safe, tested and therefore provided the most  
30 appropriate treatment.  
31  
32  
33  
34  
35

36 I'm all for these things...it might not be good for you, It might not, I don't know I  
37 can't see how because if they're now gonna put four different pills into one they  
38 musta investigated a, b, c and d to put them in one so therefore it's going to be  
39 beneficial to me and anybody else that wants those four in one (pp11, Male, 73yrs).  
40  
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### 48 **Polypill concerns**

49 Survivors' and caregivers' concerns included polypill noncompliance resulting in missing all  
50 medications, inability to adjust dosage, whether a polypill could maintain the benefits of the  
51 survivors' current secondary prevention medication, timing of a polypill, identifying the  
52 source of polypill side effects and modifying treatment if a component was no longer  
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3 required. GPs questioned whether a single pill could treat the entire stroke population, the  
4  
5 cost implications of treatment and the wisdom in modifying a patient's stable treatment  
6  
7 regimen.  
8  
9

#### 10 11 Appropriateness of treatment

12  
13 Several survivors expressed concern that a polypill may not sustain equivalent therapeutic  
14  
15 benefit of secondary prevention treatment.  
16  
17

18  
19  
20 As far as I'm concerned you've got one tablet with all the ingredients of the  
21  
22 others... if I've got the same erm dosage of statin and if it didn't disturb my  
23  
24 readings then yeah I mean erm what are the objections to it? (pp05, Male, 64 yrs)  
25  
26  
27

28  
29 Others also had concerns about the prospect of a 'pill for all', inability to alter dosage and  
30  
31 being less amenable to dose titration, if that was required.  
32  
33

34  
35  
36 Would the polypill be in different strengths because like for blood pressure at the  
37  
38 moment I'm taking...12 and a half, and then me cl- clopidogrel is 75..., maybe six  
39  
40 months down the line my blood pressure can reduce, what would that do with the  
41  
42 polypill? (pp21, Female, 68 yrs)  
43  
44  
45

46  
47 Survivors accustomed to scheduled medication regimens also questioned how drugs could  
48  
49 now be combined and taken at a single time point.  
50

51  
52 if you've got them altogether and you're supposed to take those tablets at different  
53  
54 times of the day, how's it going to work? Is it going to upset your system? (pp22,  
55  
56 Female, 71 yrs).  
57  
58  
59  
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4  
5 Suitability of the polypill strategy  
6

7 Survivors questioned the ease of managing treatment if one or more components were no  
8  
9 longer required.  
10

11       Would it only be suitable for somebody who's taking four of that particular  
12 medication? But what would happen if say the Dr said, you're not so bad so you  
13 don't need to take that particular tablet? (pp16, Female, 82 yrs)  
14  
15  
16  
17  
18  
19

20 A few expressed concerns around the inclusion of statins in any combination pill.  
21

22       Yes has that got anything to do with statins? I've read a lot about statins and I'm  
23 afraid I feel I wouldn't want to take them. Because the side effects and everything.  
24  
25  
26  
27  
28  
29 (pp19, Female, carer)  
30  
31  
32  
33

34 GPs were cautious, suggesting a polypill could be better suited to those on similar  
35 medications whose treatment was well-established.  
36  
37  
38  
39  
40

41       I think the right drugs in the right combinations there, it, would potentially be helpful  
42 for a cohort of people. I don't think it will be for everyone but there will be a cohort  
43 of people who will probably be on very similar drugs... (GP03, Male)  
44  
45  
46  
47  
48

49 Survivors and carers were also concerned that poor adherence would lead to missing all their  
50 secondary prevention drugs.  
51

52       If you're gonna give them a polypill that is three or four tablets and they don't bother  
53 taking that..They're gonna be worse off (pp14, Male, Carer)  
54  
55  
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5 Given the unique needs of stroke survivors, some suggested that multiple polypills may be  
6  
7 needed.  
8  
9

10  
11 They don't give me three separate ones for no reason, there must be a reason for it.

12  
13 You can't do that with a polypill unless you have a hundred polypills all different  
14  
15 medications and different combinations (pp18, Male, 88 yrs).  
16  
17  
18  
19

#### 20 21 Polypill side effects

22  
23 The likelihood of polypill side effects led many to question the suitability of single pill  
24  
25 treatment.  
26  
27

28  
29 The fine tuning takes a bit of doing so w- with the one pill I got my bit of a doubt that  
30  
31 it might work for some people but it might not work for everybody you see (pp04,  
32  
33 Male, 80 yrs).  
34  
35  
36  
37

38  
39 For GPs, a further problem resulting from this was the potential difficulty in identifying the  
40  
41 component of a polypill responsible for side effects.  
42  
43  
44

45 My personal anxiety is about side effects when you club two, three medicines  
46  
47 together, if one of them, one of the components is, is causing the side effect then  
48  
49 you'll not know, you may have to again change.. (GP 05, Male)  
50  
51

#### 52 53 Medication adjustment

54  
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3 GPs questioned the benefit in altering established medication routines to accommodate a  
4  
5 polypill in those who were already taking their medication as directed.  
6

7 If you've got, as I said, a very motivated patient they are happy with what they are  
8  
9 taking, then we don't probably have to intervene, but we may have to give to people  
10  
11 who are not that motivated or compliant. (GP 05, Male)  
12

13  
14  
15  
16 They also expressed concern about the inconvenience of having to re-adjust future treatment  
17  
18 if polypill components were no longer required.  
19

20  
21  
22  
23 If somebody has a problem ok well we'll just stop using the polypill and give them  
24  
25 the individual ones but with that stopping and chopping and changing people will say  
26  
27 they've changed my tablets again, that becomes an issue. (GP 04, Male)  
28

29  
30  
31  
32 However, inflexibility of a polypill and the inability to manipulate dosage was perhaps the  
33  
34 greatest concern among GPs.  
35

36 We do switch around quite a bit different brands, different sizes, statins and  
37  
38 sometimes it may not be the right dose but you kind of slowly edge it in... It would  
39  
40 be advantageous if it was a single pill but that would be maybe a bit difficult with  
41  
42 polypill...It's the fine tuning that's difficult..(GP 01, Female)  
43  
44  
45

46  
47 Caregivers also expressed concern around the inflexibility of a polypill and the potential  
48  
49 difficulties in adjusting dosage.  
50

51 You would have to get the right strengths of each tablet. "Where you were on atenolol  
52  
53 50 you are now on 25". Sometimes they change the strength of the tablet. That's  
54  
55 where it would be harder to change with the polypill (pp25, Female, carer)  
56  
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7 Size of polypill  
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9  
10 GPs raised concerns that a large pill could actually discourage medication taking.  
11

12  
13  
14 Yeah is it a horse tablet?...that's going to have the other, the opposite effect on  
15 compliance that we want...People are going to start breaking it having half now and  
16 half twelve hours later (GP 03, Male).  
17  
18  
19

20  
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22  
23 The size was also highlighted by caregivers who expressed concerns around a prospective  
24 polypill being very large.  
25  
26

27  
28  
29 Not going to be horse pills are they.. as we call them, 500 mg.  
30  
31 (pp07,Female, carer)  
32  
33

34  
35  
36 For some stroke survivors, a single pill was considered much easier given the potential  
37 problems associated with multiple medications which could be larger and more difficult to  
38 swallow.  
39  
40  
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42  
43  
44 If you can get it into one, it's so much better, you haven't got to put all these tablets  
45 down your throat. I mean like this might get stuck, and one of my tablets, if it gets  
46 stuck it burns my throat so much so the other week I lost my voice (pp06, Male, 61  
47 yrs)  
48  
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57 Cost of polypill  
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3 The burden of the polypill on NHS resources was also raised with a number of GPs  
4  
5 suggesting that a more expensive pill could be difficult to prescribe.  
6  
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9  
10 If it is cheaper then there won't be an issue at all. if it comes out to be more  
11  
12 expensive than the four tablets which you are giving individually to the patient  
13  
14 then it comes to be an issue (GP 02, Female)  
15  
16

17  
18 Cost implications for practices and pharmacies dispensing a polypill were also considered  
19  
20 with GPs acknowledging the likelihood of reduced revenues associated with a single pill.  
21  
22  
23

24  
25 They get an item fee for each thing they prescribe so if you have 4 drugs you get a  
26  
27 fee for each, if you put it in 1 pill that will account for one (GP 04, Male)  
28  
29  
30  
31  
32

### 33 34 **Polypill lessons for implementation** 35 36

37  
38 Survivors thought that whether they used a polypill in the future would depend on their  
39  
40 doctor's recommendation, but they also questioned the need for a polypill given their  
41  
42 satisfaction with current treatment. GPs acknowledged that their support was likely to be  
43  
44 influential in the decision to use a polypill and believed the approach should be adopted if it  
45  
46 was found to be beneficial to the patient. While stroke/ TIA survivors were generally positive  
47  
48 about the polypill approach, many were non-committal on its future use, largely due to the  
49  
50 lack of existing evidence.  
51  
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53  
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55  
56 Polypill recommendation  
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Caregivers felt that whether they used a polypill in the future was likely to depend on their doctor recommending the treatment.

It sounds good but w- we've got to, we would have to weigh up, listen to what the doctors say and the consultants and see what history, because this polypill, from what we've hear. Very, very little, it's quite new, that's all we know. (pp22, Male, carer)

While GP's felt comfortable with the polypill approach, there was a preference for recommending a polypill to those who were already using the medication components.

I don't think I'd be comfortable saying here's a new stroke patient, just start them with a polypill as a starting point, I think I'd feel uncomfortable with that.

If I had patients that are on the four drugs that are in there erm I think I'd probably feel fairly comfortable saying well here's one tablet that's got all of those things you're on already (GP 04, Male)

Satisfied with current medication

Being content with their current medication also made survivors less enthusiastic about taking a polypill which may have unwanted side-effects.

Why take a tablet that perhaps will affect you. Plus the fact I'm perfectly happy with what I'm on, you know, at the moment anyway. Perhaps if I go a bit doo-lally or you know erm....I would consider it (pp01, Female, 71 yrs).

1  
2  
3 While a concern raised among some study participants was that there was as yet, little  
4  
5 scientific evidence in support of a polypill approach.  
6

7  
8 No, I don't think I'd like to be a guinea pig with it though.... I don't know, I think I  
9  
10 would rather continue with what I've got until it's absolutely perfected the polypill.  
11  
12 Get somebody else (pp23, Female, 74 yrs)  
13

#### 14 15 16 Endorsement of the polypill

17  
18 GPs agreed that if they endorsed polypill, stroke/TIA survivors were likely to accept it as a  
19  
20 treatment for secondary stroke and commit to using it in the future.  
21  
22

23  
24  
25 I think the majority of our current patients if we told them we think this is the right  
26  
27 thing to do would probably be happy with that. It's a fairly easy argument (GP 03,  
28  
29 Male).  
30  
31

32  
33  
34 Furthermore, there was an obligation to try new and innovative treatments like the polypill, if  
35  
36 its potential benefits were proven.  
37  
38

39  
40  
41 I welcome change and innovation I'm excited by it... you don't know until you've  
42  
43 tried it... We have to try it if there was a potential benefit there for people (GP04,  
44  
45 Male)  
46

## 47 48 DISCUSSION

### 49 50 51 Summary of main findings

52  
53 Stroke/TIA survivors and caregivers felt a polypill offered greater convenience, reduced the  
54  
55 burden of treatment and improved adherence to medication. A polypill also ensured that  
56  
57 patients received the correct treatment and that medications were safe. However, survivors  
58  
59

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3 expressed significant concerns around the suitability of a polypill if not already using its  
4 individual components, the size of a polypill and the implication for using a polypill if any  
5 component was no longer needed. Other important limitations identified by participants  
6  
7 included the potential for side-effects and the inflexibility of the single pill approach. GPs felt  
8  
9 that a more expensive pill would be problematic and acknowledged that their endorsement  
10  
11 was key to it being accepted. For survivors, the decision to use a polypill would depend on  
12  
13 the GP's recommendation, but those who were satisfied with their current treatment regimen  
14  
15 felt less inclined to change to a polypill.  
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### 25 **Strengths and Limitations**

26  
27 A strength of this study is that it adds to a growing and important body of research on  
28  
29 attitudes towards a cardiovascular polypill with a focus on secondary prevention of stroke.  
30  
31 Second, the use of semi-structured interviews enabled an in-depth assessment of individual  
32  
33 perspectives. A further strength is the inclusion of caregivers, who can make a significant  
34  
35 contribution in the future management of polypill treatment. We believe that being  
36  
37 interviewed by a qualitative researcher rather than a health care professional encouraged  
38  
39 survivors' to be more open and to engage in discussion.  
40  
41  
42  
43

44 However, limitations include a relatively small sample of GPs' recruited from five general  
45  
46 practice surgeries. Although every effort was made to recruit a representative sample with  
47  
48 varied disability, most survivors who responded to our request to participate were primarily  
49  
50 able bodied with no significant stroke symptoms and independently managed their own  
51  
52 medication. In addition, survivors were almost exclusively White British. With some ethnic  
53  
54 groups, particularly south Asians, known to be at considerably higher risk of cardiovascular  
55  
56 disease<sup>34</sup>, the study may have benefited from the including individuals who are considered to  
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1  
2  
3 be at a greater risk from stroke and likely to be prospective users of polypill therapy. As a  
4  
5 result, survivors in our study may not represent the wider stroke population. Furthermore,  
6  
7 only five GPs were interviewed, and their opinions may not reflect those of the GP  
8  
9 population at large. With all caregivers interviewed in the presence of a survivor, this may  
10  
11 have contributed to individuals responding in a socially desirable manner and understating  
12  
13 their true views on secondary prevention and the polypill. Investigating a polypill among  
14  
15 survivors with significant symptoms and dependent on others to organise their tablets may be  
16  
17 an area for future research in the field. Finally, future research should aim to include those  
18  
19 harder to reach groups of survivors who may benefit most from a polypill approach.  
20  
21

### 22 23 24 **Comparisons with existing literature**

25  
26  
27 The inflexibility of treatment and the potential for side-effects were considered key  
28  
29 challenges of a polypill approach. Concerns about side-effects have previously been  
30  
31 identified as influencing medication taking behaviour<sup>35</sup> and recognised as a significant  
32  
33 barrier to adherence in cardiovascular disease medication<sup>36</sup>. Our findings are also in line with  
34  
35 a recent UK primary care investigation in which patients considered a secondary prevention  
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37 polypill acceptable, but were concerned about components interacting and inflexibility of  
38  
39 treatment<sup>37</sup>. The inability to adapt polypill dosage and the suitability of fixed dose treatment  
40  
41 was a key concern for GPs in our study and has been previously reported in studies exploring  
42  
43 polypill attitudes among GPs elsewhere. A small survey of 17 practitioners in New Zealand  
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45 reported that having no choice of polypill components or doses was the thing GPs disliked  
46  
47 most about the concept of a polypill<sup>25</sup>. In another UK study of primary healthcare  
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49 professionals, inability to titrate dosage was considered a major disadvantage of the polypill  
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3 The GPs in our study agreed that cost was a potential impediment to prescribing a  
4 polypill in the future. Compared with free combination medications, FDC therapy has the  
5 potential to be relatively inexpensive due to cheaper drug costs and reduced monitoring<sup>38</sup>,  
6 and there is increasing evidence in the literature supporting the cost-effectiveness of a  
7 polypill strategy<sup>39-40</sup>. With modest costs considered a cornerstone of combination therapy<sup>41</sup>,  
8 evaluations of the cost-effectiveness of using polypills is urgently needed.  
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17 Improved adherence was recognised as a key advantage of a polypill,  
18 and survivors acknowledged that a single medication episode was easier to remember. With  
19 frequent dosing regimens<sup>42</sup> and polypharmacy associated with poor patient compliance to  
20 cardiovascular medications<sup>43 44</sup>, a polypill approach offering a simplified medication regimen  
21 has the potential to improve adherence in the treatment of cardiovascular disease<sup>45 24</sup>. Our  
22 study corroborates observations from a patient perspective on whether a polypill could  
23 improve adherence, which highlighted concerns around the efficacy of a polypill compared  
24 with current medications and the potential for side-effects<sup>24</sup>.  
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35 For caregivers, benefits of a polypill included simplifying the medication taking  
36 process and ease in organising pill boxes. In a recent study on factors that influenced  
37 caregiving and medication management, participants recognised complex medication needs  
38 as an impediment to care by increasing the demands placed on the caregiver<sup>46</sup>. Caregivers in  
39 our study recognised that a polypill approach was potentially more convenient for the  
40 pharmacy, an observation which has been confirmed in a recent qualitative investigation  
41 exploring pharmacists' views towards a cardiovascular polypill<sup>47</sup>.  
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52 Stroke/TIA survivors expressed a reluctance to adopt a future polypill strategy, citing  
53 GP approval as a key factor. This not only supports the view that cardiovascular patients were  
54 inclined to do what their GPs told them<sup>48</sup> but also highlights the key role GPs can play in  
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3 promoting a polypill approach. Exploring the perspectives of those with direct experience of  
4 the polypill can contribute to the wider acceptability of a polypill strategy and should  
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6  
7 continue to be a priority of future research. While a polypill was acceptable to most patients  
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9  
10 of the UMPIRE trial, some felt that fixed-dose combination therapy was less tailored to  
11  
12 individual patient needs <sup>49</sup>. A recent investigation of the views of cardiovascular patients and  
13  
14 providers who participated in polypill trials reported similar advantages and concerns to those  
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16 identified in our study <sup>50</sup>, suggesting that polypill perspectives translate to other regions and  
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18 health care settings.  
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20  
21 With research suggesting that health practitioners often fail to fully explain the  
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23 important elements of medication when first prescribing treatment, <sup>51</sup> uptake of a polypill  
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25 may depend not only on the GP prescribing therapy but also on informing and encouraging  
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27 acceptance of the approach among stroke/TIA survivors and their caregivers.  
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### 30 31 **Implications for clinical practice** 32

33  
34 This study identified some positive aspects of a cardiovascular polypill for the  
35  
36 secondary prevention of stroke. However greater efforts are needed within the clinical  
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38 practice setting to reassure patients of the benefits of a polypill. Health professionals  
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40 endorsement when prescribing a polypill could also lead to greater acceptance of this  
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42 treatment approach and its use among stroke survivors, particularly as inadequate information  
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44 and difficulties with new medications are associated with poor adherence <sup>52</sup>. Further studies  
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46 are needed with a broader sample of GPs to corroborate the findings reported here. With  
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48 adherence among stroke survivors known to be suboptimal <sup>29</sup>, this patient group may be  
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50 particularly suited to receiving treatment using fixed-dose combination polypill therapy.  
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53 Further research on the efficacy of a polypill will also reassure practitioners whose concerns  
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3 around inflexibility and the suitability of treatment are likely to influence the decision to  
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5 prescribe a polypill to stroke/TIA survivors.  
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## 10 11 **Conclusion**

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14 A growing body of evidence suggests that a fixed-dose combination pill may have a  
15  
16 role to play in the prevention of cardiovascular disease. This study contributes to the growing  
17  
18 literature on cardiovascular polypills, offers a unique insight into the field of stroke, and may  
19  
20 inform future research and clinical practice on secondary prevention in the UK. A polypill  
21  
22 may also have a role to play in improving adherence among stroke survivors. The findings  
23  
24 have informed the development of PROPS - Preventative Role of a fixed dose combination  
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26 Pill in Stroke -, a multi-centre open label randomised controlled trial of a fixed dose  
27  
28 combination pill versus standard care for secondary prevention of stroke in a primary care  
29  
30 setting. (EudraCT number: 201300472229). However, addressing patients' and practitioners'  
31  
32 concerns and intensifying efforts to increase the acceptability of this treatment approach is  
33  
34 likely to determine future use of a cardiovascular polypill for the secondary prevention of  
35  
36 stroke.  
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## 40 41 **Acknowledgements**

42  
43  
44 The authors wish to thank the stroke/TIA survivors, caregivers and general practitioners who  
45  
46 agreed to be interviewed, the GP surgeries who participated in this research and the Primary  
47  
48 Care Research Network co-ordinator for assisting with recruitment.  
49  
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## 51 52 **Competing Interests**

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55 None declared.  
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### Author/s contribution

Jonathan Mant conceived the study, is the chief investigator on the polypill programme and commented on the final draft of the manuscript. Jonathan Graffy is a co-investigator on the polypill programme, contributed to the data analysis and commented on the manuscript.

Ricky Mullis is a co-investigator on the polypill programme, contributed to developing the study protocol and commented on the manuscript. Stephen Sutton is a co-investigator on the polypill programme, contributed to the data analysis and commented on the manuscript.

James Jamison contributed to developing the study protocol, conducted the interviews and data analysis and prepared the manuscript for submission.

### Data sharing

No additional data available.

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<b>Gender</b>	Male: n=21 (75%) Female: n=7 (25%)
<b>Age (Mean: 74yrs)</b>	60-69yrs: n=10 (36%) 70-79yrs: n=11 (39%) 80-89yrs: n=7 (25%)
<b>Ethnicity</b>	White: n=27 (97%), South Asian: n=1 (3%)
<b>Stroke classification</b>	Stroke: n=14 (50%) TIA: n=14 (50%)
<b>Time since stroke</b>	6 mths-2 yrs: n=10 (35%) 3-5 yrs: n=8 (29%) 6-10 yrs: n=5 (18%) >10 yrs: n=5 (18%)
<b>Diabetes status</b>	Yes: n=9 (32%) No: n=19 (68%)
<b>Smoking status</b>	Non-smoker: n=15 (54%) Ex-smoker: n=11 (39%) Smoker: n=2 (7%)
<b>Interview status</b>	Survivor and caregiver: n=14 (50%) Survivor only: n=14 (50%)
<b>Rankin score*</b>	No symptoms: (0) n=6 (21%)
<b>MrS-9Q</b>	No sig. disability: (1) n=4 (14%)

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	Slight disability: (2) n=6 (21%)
	Moderate disability: (3) n=4 (14%)
	Mod severe/ severe disability: (4-5) n=8 (29%)

Table 1. Stroke survivor characteristics. \*Rankin score is derived from a scale that measures the degree of disability in the daily activities of people who may have suffered a stroke

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## Supplementary File 1

## Topic guide for semi-structured interviews

## Stroke survivors

**Can you tell me a bit about your experience of having a stroke?**

What were you advised to do? What do you know about the risk factors for having another stroke?

**Taking your medication?**

Can you tell me about your current medication taking experience? Any difficulties?

**Do you know what a polypill is?**

What do you think of being able to take a single pill (containing a combination of different stroke medications in one pill) instead of your usual medication?

How do you think this would change the experience of taking medication?

What would you consider to be the advantages of taking a polypill?

Can you think of any reasons why taking a polypill might not be a good thing?

Would you consider taking a polypill in the future?

**Can you tell me about your relationship with your GP?**Carers**Can you tell me about your experience of being a carer?**

How informed do you feel you are? about your stroke survivors condition?

**Do you manage the medication? Can you tell me about this?**

Are there any specific difficulties related to patient taking the stroke medication?

Can you think of any ways in which the medication taking process could be made easier/improved?

**Have you heard of a polypill?**

What do you think of the idea of a 'polypill'?

What do you think of the patient taking a single polypill instead of their usual stroke medications?

How do you think this would benefit patient's medication taking behaviour?

Can you think of any reasons why taking a polypill may not be a good idea?

How do you think a polypill would enable better management of medication?

Can you think of any ways taking polypill would be a disadvantage?

What do you think about using a polypill in the future?

GPs**Current Practice**

Can you tell me about current practice for secondary prevention of stroke?

Can you think of any limitations associated with current practice?

**Polypill**

What do you know about polypill therapies? - for treating cardiovascular disease?

Are you familiar with these?

What do you think about using a polypill for secondary prevention? Do you think it's feasible?

What would be the difficulties (if any) with using polypill for secondary prevention?

If a polypill became available for secondary prevention, is it something you would consider using?

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## Consolidated criteria for reporting qualitative studies (COREQ): 32-item checklist

No	Item	Guide questions/description	
<b>Domain 1: Research team and reflexivity</b>			
Personal Characteristics			
1.	Interviewer/facilitator	Which author/s conducted the interview or focus group?	JJ was the interviewer
2.	Credentials	What were the researcher's credentials? <i>E.g. PhD, MD</i>	BSc, MSc
3.	Occupation	What was their occupation at the time of the study?	Research Assistant/ PhD Student
4.	Gender	Was the researcher male or female?	Male
5.	Experience and training	What experience or training did the researcher have?	JJ is a researcher with experience in undertaking qualitative research.
Relationship with participants			
6.	Relationship established	Was a relationship established prior to study commencement?	No
7.	Participant knowledge of the interviewer	What did the participants know about the researcher? <i>e.g. personal goals, reasons for doing the research</i>	Participants were informed that the researcher was a PhD student who worked for the University of Cambridge
8.	Interviewer characteristics	What characteristics were reported about the interviewer/facilitator? <i>e.g. Bias, assumptions, reasons and interests in the research topic</i>	Participants know that the researcher works in a primary care unit and is investigating as new approach to secondary stroke prevention using a Polypill
<b>Domain 2: study design</b>			
Theoretical framework			
9.	Methodological orientation and Theory	What methodological orientation was stated to underpin the study? <i>e.g. grounded theory, discourse analysis, ethnography, phenomenology, content</i>	Grounded Theory

No	Item	Guide questions/description	
		<i>analysis</i>	
Participant selection			
10.	Sampling	How were participants selected? <i>e.g. purposive, convenience, consecutive, snowball</i>	Purposive/ convenience sampling –stroke survivors were selected purposively in order to achieve a range of gender, socio economic status, stroke severity. Caregivers and GPs were a convenience sample recruited through the survivors and as the GP leading the study within the practice, respectively.
11.	Method of approach	How were participants approached? <i>e.g. face-to-face, telephone, mail, email</i>	Stroke survivors were approached by letter. Carers were approached directly through the stroke survivor. GPs were approached by phone.
12.	Sample size	How many participants were in the study?	28 stroke survivors, 14 caregivers, 5 GPs
13.	Non-participation	How many people refused to participate or dropped out? Reasons?	No one refused to participate
Setting			
14.	Setting of data collection	Where was the data collected? <i>e.g. home, clinic, workplace</i>	Data was collected in the patients/caregivers home and in the GPs place of work
15.	Presence of non-participants	Was anyone else present besides the participants and researchers?	Other than the caregiver who participated in joint interviews, no-one else was present during the interview..
16.	Description of sample	What are the important characteristics of the sample? <i>e.g. demographic data, date</i>	Gender, stroke status, age
Data collection			
17.	Interview guide	Were questions, prompts, guides provided by the authors? Was it pilot tested?	Yes. An interview guide was developed for survivors, caregivers and GPs. Guides were tested by 2 stroke survivors and a clinical researcher commented on the GP guide.
18.	Repeat interviews	Were repeat interviews carried out? If yes, how	No

No	Item	Guide questions/description	
		many?	
19.	Audio/visual recording	Did the research use audio or visual recording to collect the data?	Yes. All interviews were audio recorded.
20.	Field notes	Were field notes made during and/or after the interview or focus group?	Yes. Field notes were taken during interviews.
21.	Duration	What was the duration of the interviews or focus group?	Interviews lasted between 1 and 1.5 hours
22.	Data saturation	Was data saturation discussed?	Yes
23.	Transcripts returned	Were transcripts returned to participants for comment and/or correction?	No
<b>Domain 3: analysis and findings</b>			
Data analysis			
24.	Number of data coders	How many data coders coded the data?	2 authors contributed to the coding process. JJ coded all of the interviews. 20% were also coded independently by SS.
25.	Description of the coding tree	Did authors provide a description of the coding tree?	Not explicitly
26.	Derivation of themes	Were themes identified in advance or derived from the data?	Themes were generated from the data
27.	Software	What software, if applicable, was used to manage the data?	Nvivo 9
28.	Participant checking	Did participants provide feedback on the findings?	No.
Reporting			
29.	Quotations presented	Were participant quotations presented to illustrate the themes / findings? Was each quotation identified? e.g. <i>participant number</i>	Yes, quotations were presented in the text to illustrate the themes.. Participants were identified by a number.
30.	Data and findings consistent	Was there consistency between the data presented and the findings?	Yes
31.	Clarity of major	Were major themes clearly	Yes

No	Item	Guide questions/description	
	themes	presented in the findings?	
32.	Clarity of minor themes	Is there a description of diverse cases or discussion of minor themes?	Yes. Both key themes and sub-themes are reported. Restrictions on word count prevented themes being discussed extensively

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