

# 1 Attitudes Toward Using Single-Pill Combination (Polypill) Therapy in Heart 2 Failure: Patients' and Physicians' Perspectives

3 Polypill Therapy in Heart Failure

4

5 Jan Biegus<sup>1,2</sup>, Rafał Tymków<sup>1</sup>, Javed Butler<sup>3,4</sup>, Marco Metra<sup>5</sup>, Ovidiu Chioncel<sup>6</sup>, Vijay Chopra<sup>7</sup>,  
6 Marianna Adamo<sup>8</sup>, Julio Nuñez<sup>9</sup>, Giuseppe Rosano<sup>10,11</sup>, Clara Saldarriaga<sup>12</sup>, Michael Böhm<sup>13</sup>,  
7 Shelley Zieroth<sup>14</sup>, Piotr Ponikowski<sup>1,2</sup>.

8

9 1-Jan Mikulicz Radecki University Hospital in Wrocław, Poland

10 2-Department of Cardiology, Clinical Department of Intensive Cardiac Care, Wrocław Medical  
11 University, Faculty of Medicine, Institute of Heart Diseases, Wrocław, Poland

12 3- Baylor Scott and White Research Institute, Dallas, Texas, USA

13 4-University of Mississippi, Jackson, MS

14 5-Institute of Cardiology, ASST Spedali Civili, Department of Medical and Surgical Specialties,  
15 Radiologic Sciences and Public Health, University of Brescia, Brescia, Italy

16 6-Emergency Institute for Cardiovascular Diseases "Prof. C.C.Iliescu", University of Medicine  
17 "Carol Davila," Bucharest, Romania

18 7-Deptt of Cardiology, Max Super Speciality Hospital, Saket, New Delhi

1 8-Institute of Cardiology, ASST Spedali Civili, Department of Medical and Surgical Specialties,  
2 Radiologic Sciences and Public Health, University of Brescia, Brescia, Italy

3 9-Department of Cardiology, Hospital Clínico Universitario de Valencia, Spain, Department of  
4 Medicine, Valencia, Spain

5 10-Department of Human Sciences and Promotion of Quality of Life, San Raffaele Open  
6 University of Rome, Rome, Italy

7 11-IRCCS San Raffaele Roma, Rome, Italy

8 12-Department of cardiology CardioVID CLINIC, Pontificia Bolivariana University, Medellín-  
9 Colombia

10 13-HOMICAREM (HOMburg Institute for CARDioREnalMetabolic Medicine) and Klinik für  
11 Innere Medizin III, Saarland University, Medical Faculty, Kirrberger Str.1, 66421 Homburg/Saar,  
12 Germany Saarland University

13 14-Section of Cardiology, Max Rady College of Medicine, University of Manitoba, Winnipeg,  
14 Manitoba, Canada

15

16 **CORRESPONDING AUTHOR:**

17 Dr Jan Biegus, MD, PhD

18 Institute of Heart Diseases, Wrocław Medical University,

19 50-556 Wrocław, Borowska 213, Poland

20 Tel: +48-71-733 11 12

21 e-mail: [jan.biegus@umw.edu.pl](mailto:jan.biegus@umw.edu.pl)

1 Twitter: @JanBiegus

## 2 **Attitudes Toward Using Single-Pill Combination (Polypill) Therapy in Heart** 3 **Failure: Patients' and Physicians' Perspectives**

### 4 5 **Abstract**

#### 6 **Background:**

7 Single-pill combinations (SPC, *polypills*) have proven effective in cardiovascular areas, yet no  
8 such therapy exists for patients with heart failure (HF) despite substantial polypharmacy and pill  
9 burden in this population. Simplifying treatment through an HF-specific SPC containing key  
10 guideline-directed medical therapy (GDMT) components could improve adherence and  
11 outcomes.

#### 12 **Methods:**

13 Two prospective, electronic surveys were conducted between June and October 2025 to assess  
14 real-world attitudes toward a polypill in HF with ejection fraction  $\leq 50\%$ . The physician-oriented  
15 survey (22 questions) was distributed internationally and explored GDMT practices, perceived  
16 needs, barriers, and potential preferred composition of an HF dedicated SPC. The patient-  
17 oriented survey (11 questions) explored medication burden, adherence, and perceptions of a  
18 potential polypill use.

#### 19 **Results:**

20 A total of 250 physicians and 126 patients participated. Among physicians, 77% reported a clear  
21 need for strategies to simplify GDMT optimization in HFrEF, with cost (66%) and polypharmacy

1 (54%) being selected as the most frequent barriers. Nearly all physicians (95%) recognized a real  
2 clinical need for an HF-specific SPC, and most perceived it as clinically useful (88%),  
3 logistically feasible (76%), and acceptable to patients (94%). Approximately 48% of physicians  
4 declared that they would use it regularly, and another 49% would use it in selected patients. The  
5 preferred composition of HF-specific SPC included a beta-blocker, mineralocorticoid receptor  
6 antagonist (MRA), and SGLT2 inhibitor (61.2%).

7 Among patients, polypharmacy was common (70% taking  $\geq 6$  drugs daily), and 75% admitted to  
8 occasional non-adherence. Most responders (82%) would support a solution that reduces the pill  
9 burden, and 83% would take an HF-specific SCP if offered, particularly if there is no extra cost.

## 10 **Conclusions:**

11 Both physicians and patients showed strong openness and willingness toward an HF-specific  
12 SPC, supporting further development and evaluation of HF-specific polypill strategies.

13

14 Keywords: GDMT, polypill, single-pill combination,

15 Wordcount: 4021

16

## 17 **Introduction**

18 Single-pill combination (SPC, polypill) therapy has been shown to be useful and effective in  
19 several cardiovascular areas, such as hypertension, coronary atherosclerotic disease, and  
20 prevention<sup>1-4</sup>. However, polypills for heart failure (HF) patients are not. This contrasts with the  
21 fact that HF seems to be a perfect setting for a polypill approach, as polypharmacy is common

1 and the pill burden is substantial<sup>5</sup>. HF patients, particularly those with HFrEF (HF with reduced  
2 ejection fraction), are recommended to take drugs from at least four (if not five) major drug  
3 classes<sup>6</sup>. Therefore, the polypill concept appears highly attractive for these patients. From a  
4 theoretical perspective, the polypill may provide several benefits over the standard approach,  
5 with each drug being prescribed as a separate pill, from both the patient's and the physician's  
6 perspective. These include, but are not limited to, greater ease of administration and a reduced  
7 pill burden, resulting in improved treatment adherence, which, in the long term, may translate to  
8 improved outcomes.

9 This study aimed to examine the real-world attitudes of patients and physicians toward the  
10 single-pill combination concept in HF.

## 11 **Methods**

12 We conducted two separate prospective, electronic surveys to examine attitudes toward the  
13 polypill concept. The physician-oriented survey was written in English and contained five major  
14 domains: respondent information, HF guideline-directed medical therapy (GDMT) treatment  
15 questions, polypill questions, polypill in HF – potentially optimal composition, and the potential  
16 population for the polypill questions. The physician's survey consisted of 22 questions in total. In  
17 the introduction to the survey, respondents were informed that the survey pertained to the  
18 management of patients with HF and a reduced or mildly reduced ejection fraction (LVEF  
19 <50%). The survey is available at: <https://forms.gle/Fi8wfkUR5RuifhTTA>. The authors of the  
20 paper disseminated the physician survey within their professional community. The survey was  
21 disseminated from June 2025 to October 2025.

1 The patient-oriented survey was written in Polish, and only Polish patients responded. It included  
2 three main areas: questions to characterize the respondent, the respondent's pill burden and  
3 adherence, and their opinion on the polypill concept, with a total of 11 questions. The patient's  
4 survey was deliberately short to make it more responder-friendly. We gathered the survey  
5 responses from June 2025 to October 2025. The survey is available at:  
6 <https://forms.gle/r9K6RCShnGSWWRig7>. All participants' responses were kept anonymous, and  
7 their participation was voluntary.

8 The data are presented as numbers and percentages of the total population. No statistical analyses  
9 were performed.

## 10 **Results**

### 11 *Physician-targeted survey*

12 From June 2025 to October 2025, a total of 250 physicians responded to the survey. The majority  
13 of them were from Europe (n=207, 82.8%) and South/Central America (8%); the other regions  
14 included North America and Asia. The majority of responders were cardiologists (80.4%), HF  
15 specialists (8.4%), and internists (5.2%). The responders had significant clinical experience (>20  
16 years of practice declared by 24%, 11-20 years of practice: 30.4%, 5-10 years of practice: 22.8%,  
17 and <5 years: 22.8%). The physicians worked primarily in academic hospitals (77.6%) or  
18 public/non-academic facilities (13.6%). The majority of responders managed a substantial  
19 number of HF<sub>r</sub>EF/HF<sub>m</sub>rEF patients per week: 31-50/week (8.8%), 21-30/week (14.4%), 10-  
20 20/week (46.4%), <10/week (25.2%).

21 A majority of physicians (n=193, 77.2%) agreed "definitely" with the statement that "there is a  
22 need for strategies to improve and simplify the optimization of GDMT in patients with

1 HFrEF/HFmrEF”, while the rest answered “possibly”. The most common barriers to the optimal  
2 implementation of GDMT in HF reported by the responders were cost of medications (n=164,  
3 65.5%), polypharmacy (n=134, 53.6%), adverse effects or drug intolerance (n=118, 47.2%),  
4 insufficient follow-up opportunities for medication optimization (n=110, 44%).

5 The majority of respondents (49.6%) recognized a clear need for a SPC that combines key  
6 GDMT components for patients with HF and LVEF <50%. The other 115 physicians (46%)  
7 indicated that the need might depend on the patient's profile (Figure 1). Almost all responders  
8 (n=226, 90.4%) agreed (49.2%) or strongly agreed (41.2%) that the HF-specific SPC would  
9 improve adherence. Most respondents perceived the polypill as clinically useful (n=218, 87.2%),  
10 logistically feasible (n=190, 76.0%), and acceptable to patients (n=233, 93.2%) (Figure 2).

11 A total of 123 physicians (48.4%) indicated they would use the HF polypill regularly, 121  
12 (49.2%) would use it only in selected patients, while just 3 (1.2%) responded negatively, and 3  
13 (1.2%) were unsure. The top three pieces of evidence that responders considered essential to  
14 support the use of the polypill in their practice were: real-world data confirming higher  
15 adherence and safety (n=155, 62%), a randomized controlled trial demonstrating clinical efficacy  
16 (n=137, 54.8%), and health-economic data showing cost-effectiveness (n=95, 38%).

17 The top three concerns regarding the use of the polypill in HF were: tolerability/safety concerns  
18 (n=161, 64.4%), reimbursement and cost (37.6%), and limited clinical trial evidence (18.8%).

19 Most of the respondents support the concept of a polypill in HF patients, with 235 (94%)  
20 welcoming a polypill as an additional treatment option, n=213 (85.2%) felt that polypill was a  
21 good match for their patients, and n=211 (84.4%) would prefer HF-specific SPC over the usual  
22 care for stable patients (Figure 3).

1 Most physicians indicated that the polypill should contain three components (49.6%), while 85  
2 (34%) responders selected four components, 30 (12%) selected two components, and the  
3 remaining 11 (4.4%) selected five components (Figure 4a). The top selected combination of the  
4 GDMT that HFrEF/HFmrEF polypill should contain was beta-blocker+MRA+SGLT-2i (n=153,  
5 61.2%), ARNI+MRA+SGLT-2i (n=70, 28%), and beta-blocker+ACEI+SGLT-2i (n=64, 25.6%).  
6 The same combination (beta-blocker+MRA+SGLT-2i) was indicated as the most likely  
7 considered as a treatment option for patients with HFrEF by 175 (70%) of the responders (Figure  
8 4b).

9 Regarding the timing of the potential prescribing of the polypill “the outpatient/community  
10 setting, once a patient is on stable doses of GDMT” was the most frequently selected option,  
11 followed by the “at time of hospital discharge” and “during hospitalization”, n=188 (75.2%);  
12 n=109 (43.6%) and n=71 (28.4%), respectively. The polypill would be most strongly considered  
13 by physicians for patients with poor adherence (n=174, 69.9%), patients with polypharmacy  
14 (n=161, 64.4%), and in all HF patients (n=91, 36.4%). On the other hand, the top three selected  
15 populations for whom the polypill would not be suitable or indicated were: frail patients (n=115,  
16 46%), patients with multiple comorbidities (n=108, 43.2%), and the elderly population (n=71,  
17 28.4%).

18 The largest proportion of respondents (34.8%) estimated they would offer the polypill to 26–50%  
19 of their HFrEF patients, followed by (28.0%) for 51-75%, (18.0%) for >75%, and (15.2%) for  
20 10-25%, while only a minority (4%) selected <10% (Figure 5).

21

22 *Patient-targeted survey*

1 A total of 126 patients responded to the survey. The polypharmacy was very frequent. The  
2 majority of patients (n=88, 69.8%) reported receiving  $\geq 6$  medications daily, 21 (16.7%) selected  
3 five medications, and the remaining 17 (13.3%) declared taking  $\leq 4$  medications daily. The  
4 medications were taken most often twice daily (n=59, 46.8%), followed by three times per day  
5 (n=55, 43.7%).

6 Almost  $\frac{3}{4}$  of patients reported missing their medications, with the frequency categorized as  
7 rarely (defined as 1-2 times per month) (46.8%); sometimes (defined as 1-2 times per week)  
8 (18.3%); or frequently ( $>3$  times per week), (4.8%). The remaining 38 (30.2%) patients declared  
9 that they never miss their medications. Most responders (58.7%) indicated that daily medication  
10 intake was not an issue; however, 31% found it problematic, and 10.3% were unsure and chose  
11 "hard to say." Analogously, the frequency of medication intake was not perceived as a significant  
12 burden by 64 patients (50.8%). In contrast, 40.5% selected it as a significant burden, and 8.7%  
13 chose the "hard to say" answer. Notably, 25 patients (19.8%) reported missing some of their  
14 medications due to the number or high frequency of intake.

15 Forty-five (35.7%) patients selected that the high number of medications taken daily negatively  
16 impacts their well-being or everyday living activities, while n=15 (11.9%) had no opinion on this  
17 issue.

18 Importantly, the majority of patients (81.7%) expressed interest in solutions that reduce the  
19 number of tables daily (i.e., SPC) (Figure 6a). Moreover, 87 responders (69%) would like their  
20 physician to offer them a solution that simplifies adherence and compliance, while only five  
21 responders (4%) would not welcome it. Most patients (n=105, 83.3%) would like their physician  
22 to offer them a polypill, and they would be likely to take it if there were no additional cost  
23 associated with the solution. While only 5.6% would not like that offer, and 11.1% selected "hard

1 to say” answer (Figure 6b). Lastly, the majority of patients (57.1%) believe that the polypill  
2 would improve their everyday medication adherence, while 22.2% think it would not change  
3 adherence, and 20.6% have no opinion on the matter.

#### 4 **Discussion**

5 The two surveys demonstrated that both physicians and patients favor polypills for therapeutic  
6 simplification. Notably, the majority of physicians (~77%) reported a need for strategies to  
7 improve and simplify the optimization of GDMT in patients with HF<sub>rEF</sub>/HF<sub>mrEF</sub>. This indeed  
8 seems to be an unmet need in the pharmacotherapy of HF patients. At the same time, we must  
9 emphasize that polypharmacy (the need to take  $\geq 5$  medications) was the second most common  
10 (after cost of medications) barrier that the physicians selected to optimize the implementation of  
11 GDMT. The patients' reluctance to take a high daily pill burden was selected by 37% of  
12 responders. When we appreciate that HF patients often have several comorbidities, and  
13 sometimes also take other medications and supplements without clear medical indications, then  
14 we realize that the pill burden in HF is substantial<sup>7,8</sup>.

15 All the above most likely resulted in a strong openness to the single-pill combination concept,  
16 with 95% of physicians recognizing the real clinical need for a polypill combining key GDMT  
17 components for HF patients with reduced or mildly reduced ejection fraction (LVEF <50%).  
18 Notably, about 46% of respondents clearly recognized the need, whereas ~49% noted that it  
19 depends on the patient's profile and clinical context. This is also supported by the fact that most  
20 physicians believe the SPC would improve adherence, be clinically useful, logistically feasible,  
21 and acceptable to patients. Given that, almost all responders declared that they would use the  
22 HF-specific SPC in their everyday practice, either regularly (~49%) or only in selected patients  
23 (~48%).

1 Despite the evident anticipation that the polypill concept is needed for HF patients, the  
2 respondents pointed out that the main concerns regarding its use were tolerability and safety  
3 issues, cost, and the lack of clinical evidence for its effectiveness. These comments highlight the  
4 relative lack of familiarity of the physicians with the regulatory pathways for SPCs, as these  
5 combinations can be registered as both substitution therapy or as an initial approach. In the first  
6 case, no additional data is required because patients are switched from two or more drugs at a  
7 given dose to an SPC containing the same doses of the same medications. The effectiveness of an  
8 SPC containing medications currently used for the given disease is not needed if the medicines  
9 contained in the SPC are used in common practice and/or suggested by guidelines.

10 Moreover, the physicians would be less likely to initiate the SPCs in frail patients, in patients  
11 with multiple comorbidities, and in elderly patients<sup>9</sup>. On the other hand, almost half of the  
12 responders selected that they would use the polypill in more than half of their patients.

13 Moreover, although we fully agree that the above-mentioned vulnerable populations certainly  
14 require special caution during treatment, it is worth noting that in the STRONG-HF trial —  
15 where patients received high-intensity care (although, of course, this is not equivalent to a  
16 polypill approach) — no significant increase in risk was observed among elderly patients or  
17 those with multiple comorbidities<sup>10-12</sup>.

18 Interestingly, the majority of physicians selected that the polypill should contain three (not four)  
19 components, and those suggested components were: beta-blocker, MRA, and SGLT-2i. This is  
20 probably a very pragmatic option, as the inclusion of ARNi (or some ACEI), which should be  
21 taken twice daily, would be problematic in terms of simplifying the daily regimen. On the other  
22 hand, including a loop diuretic, whose dose might need adjustment based on the patient's fluid  
23 status, would make the single-pill combination less pragmatic.

1 The patient survey confirmed that HF patients' pill burden is significant, which may contribute to  
2 reduced adherence. Interestingly, only about one-third of patients reported that they never forget  
3 to take their medications, while the other report some non-adherence. However, it should be  
4 noted that for more than half of the respondents, the number of medications taken daily was not  
5 perceived as a significant issue. At the same time, one-third of patients indicated that the high  
6 number of medications negatively affects their everyday life and overall well-being.

7 Surprisingly, patients expressed significant openness to the novel concept of the polypill. The  
8 vast majority of patients expressed interest in a solution that would allow them to take fewer pills  
9 daily, and as many as 83% would like their physician to offer them a polypill for HF treatment.  
10 Lastly, nearly 60% of patients believed that such a solution would improve their daily medication  
11 adherence.

12 Lastly, our study is the first to capture the real-world attitudes and opinions of the two most  
13 important stakeholders involved in prescribing and taking medications. We are not aware of any  
14 previous studies that have examined these perspectives simultaneously. The views and behaviors  
15 of both groups are crucial for the potential success of the HF-specific SPC concept, which, from  
16 a scientific standpoint, represents an unmet need for HF patients.

17 In conclusion, physicians and patients demonstrated strong openness and anticipation toward an  
18 HF-specific SCP concept. The perceived benefits of adherence and treatment simplification  
19 might outweigh concerns regarding safety, cost. Both physicians and patients clearly declared  
20 their willingness to use the HF-specific SPC if it were available.

21 Limitations:

1 Most respondents to the survey were physicians from Europe; therefore, caution is necessary  
2 when applying the results to other populations because prescribing patterns and medication  
3 availability vary across regions<sup>13-15</sup>. Additionally, there is always some selection bias in all  
4 volunteer surveys, which also affects our research. The patient-focused examination only studied  
5 the Polish population, which presents another limitation. Our study is limited to the information  
6 that was predefined by the survey questions and, in most cases, suggested in the survey answers.  
7 The survey did not ask specific questions about the number of doses within pre-defined  
8 combinations. The survey neither asked questions that could distinguish the patient's  
9 characteristics associated with higher versus lower willingness to take polypills.

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14  
15 **Conflicts of interest:**

16 Jan Biegus has received honoraria from Bayer, Boehringer Ingelheim, and AstraZeneca for  
17 lectures and from Alleviant Medical, Reprieve Cardiovascular, and WhiteSwell for participation  
18 in clinical trial advisory boards. Jan Biegus is a member of the Editorial Board of ESC Heart  
19 Failure (Deputy Editor) and Heart Failure Reviews (Associate Editor).

20 Javed Butler reports: consultant Abbott, Adapticx, American Regent, Amgen, AskBio,  
21 AstraZeneca, Bayer, Boehringer Ingelheim, Boston Scientific, Bristol Myers Squibb, Cardiac  
22 Dimension, Cardior, CSL Vifor, CVRx, Cytokinetics, Daxor, Diastol, Edwards, Element

1 Sciences, Faraday, Idorsia, Impulse Dynamics, Imbria, Innolife, Intellia, Inventiva, Levator,  
2 Lexicon, Eli Lilly, Mankind, Medtronic, Merck, New Amsterdam, Novartis, NovoNordisk,  
3 Pfizer, Pharmacosmos, Pharmain, Prolaio, Pulnovo, Regeneron, Renibus, Reprieve, Roche,  
4 Rycarma, Saillant, Salamandra, Salubris, SC Pharma, SQ Innovation, Secretome, Sequanna,  
5 Transmural, TekkunLev, Tenex, Tricog, Ultronic, Vera, Zoll

6 Vijay Chopra received modest speaking fee from Astra, Boehringer, Novartis, Bayer, Lupin, Sun,  
7 Torrent, Mankind, Glenmark, USV, Alembic, Alkem and National Coordinators fee for clinical  
8 trials from Novartis, Boehringer, Astra

9 Shelley Zieroth has served on advisory boards or speaker engagements with AskBio, Abbott,  
10 Alnylam, AstraZeneca, Bayer, BMS, Boehringer Ingelheim, CSL Vifor, Cytokinetics, Edwards,  
11 Eli Lilly, GSK, Medtronic, Merck, Novartis, Novo-Nordisk, Pfizer, Viartis and serves on a clinical  
12 trial committee for studies sponsored by AstraZeneca, Boehringer Ingelheim, Cytokinetics, Merck,  
13 Pfizer, Salubris Bio. Non industry: CCS, CHFS, Charite, CPD Network, CSN, EOCI, Liv,  
14 Medscape, Medudy, Radcliffe, Reach MD, Sciarc, Translational Medicine Academy, Voxmedia

15 Julio Núñez has received honoraria for presentations or advisory boards from Alleviant,  
16 AstraZeneca, Boehringer Ingelheim, Bayer, Lilly, Novartis, NovoNordisk, Pfizer, Roche, Rovi,  
17 and Vifor CSL

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20 Bayer, Boehringer Ingelheim, Cytokinetics, Medtronic, Novartis, ReCor, Servier and Vifor.

21 Marianna Adamo reports speaker honoraria from Abbott Vascular and Edwards Lifesciences.

1 Clara Saldarriaga has received honoraria as advisor for Novo Nordisk, Bayer and Merck clinical  
2 trials, also as a speaker for Astrazeneca, Novartis, Boehringer Ingelheim, Pfizer, Bayer, Merck,  
3 Adium, Servier, Medtronic, Novo Nordisk, Eli Lilly.

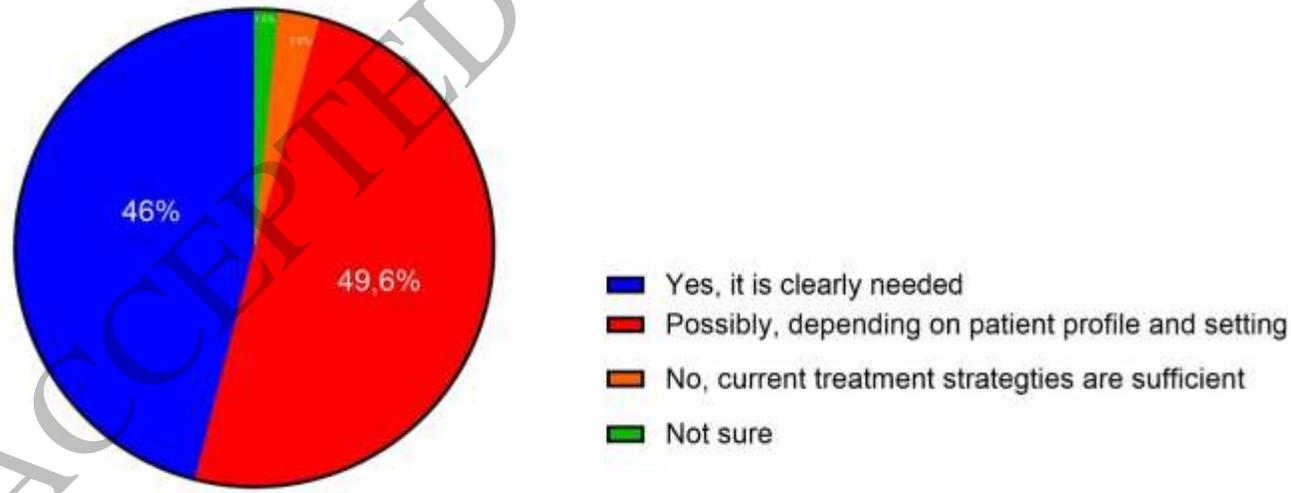
4 G.M.C.R.reports speaker fees/consultancies from AstraZeneca, Boehringer Ingelheim, CSL  
5 Vifor, Alnylam, Servier, Medtronic, Bayer, Cipla, Novartis, Viatris and Menarini.

6

7 **Figure legends.**

8 **Figure 1. Perceived need for a HF-specific single pill combination among physicians.**

9 *Responses to the question: “Do you think there is a need for a polypill combining key GDMT*  
10 *components for patients with heart failure with reduced/mildly reduced ejection fraction (LVEF*  
11 *<50%)?” (n=250).*



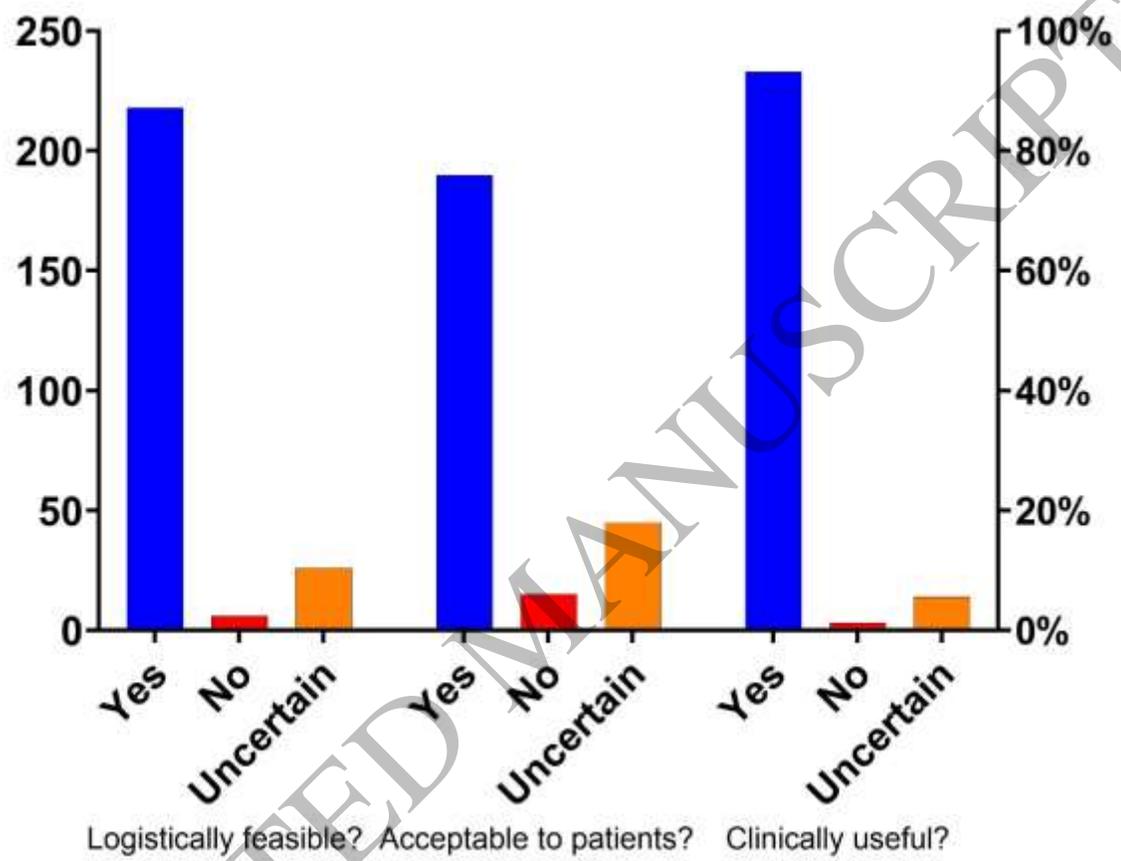
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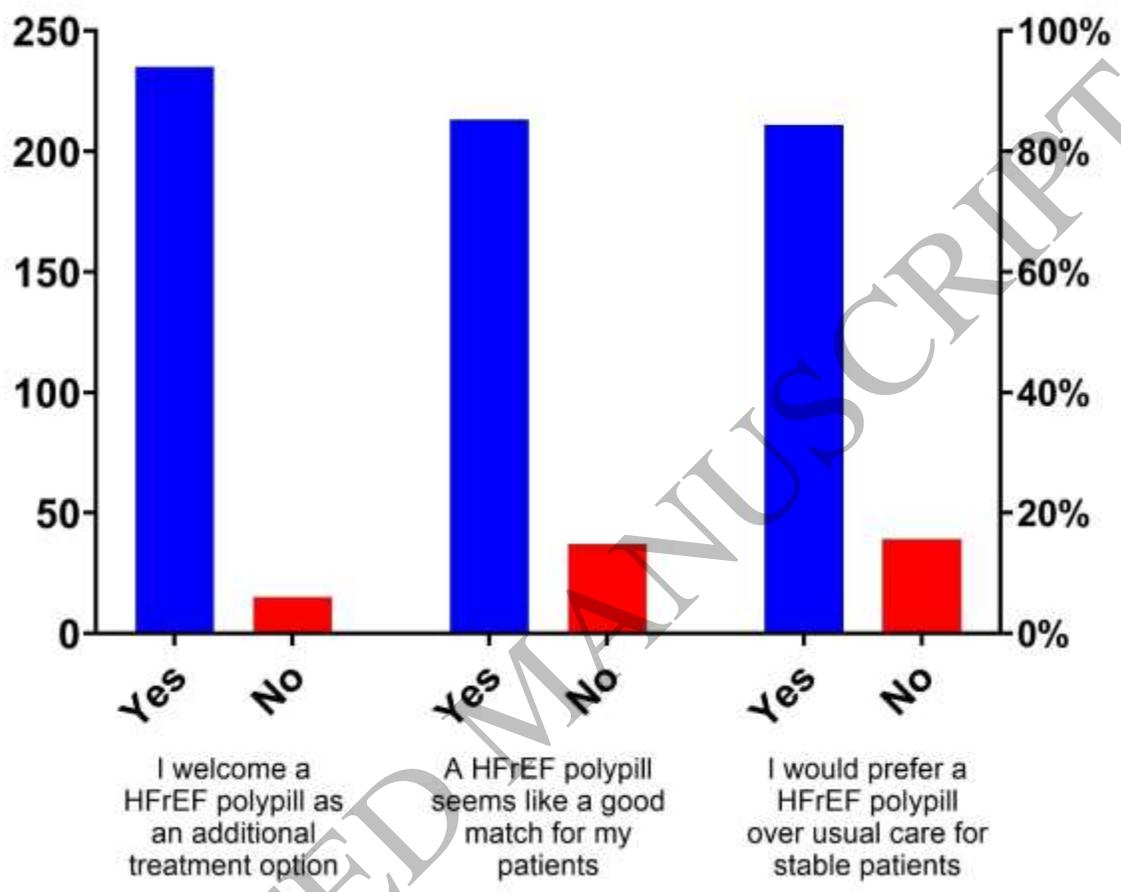
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1 Figure 2. The anticipated clinical usefulness, feasibility, and patient acceptability of an HF-  
2 specific single-pill combination.



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1 Figure 3. Physician support for the concept of an HF-specific SPC.

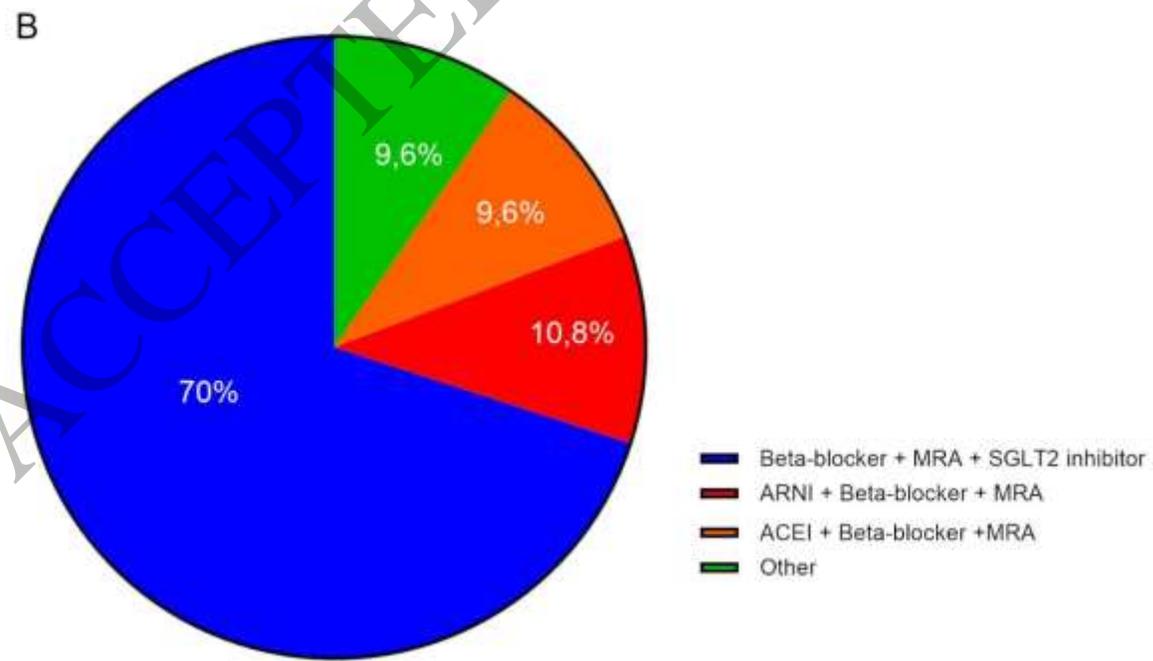
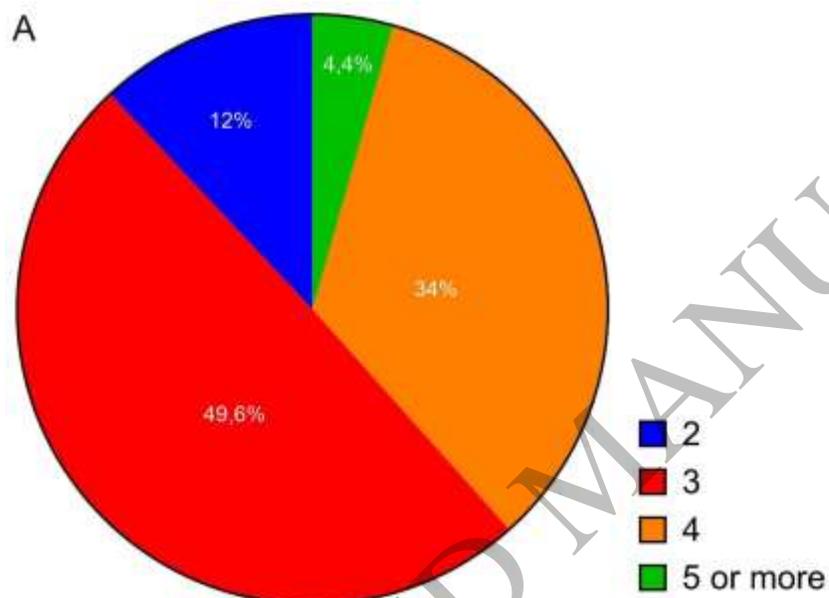


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1 **Figure 4. The components of the single-pill combination.**

2 **Figure 4a. The proposed number of active components the potential HF-specific SPC should**  
3 **contain.**

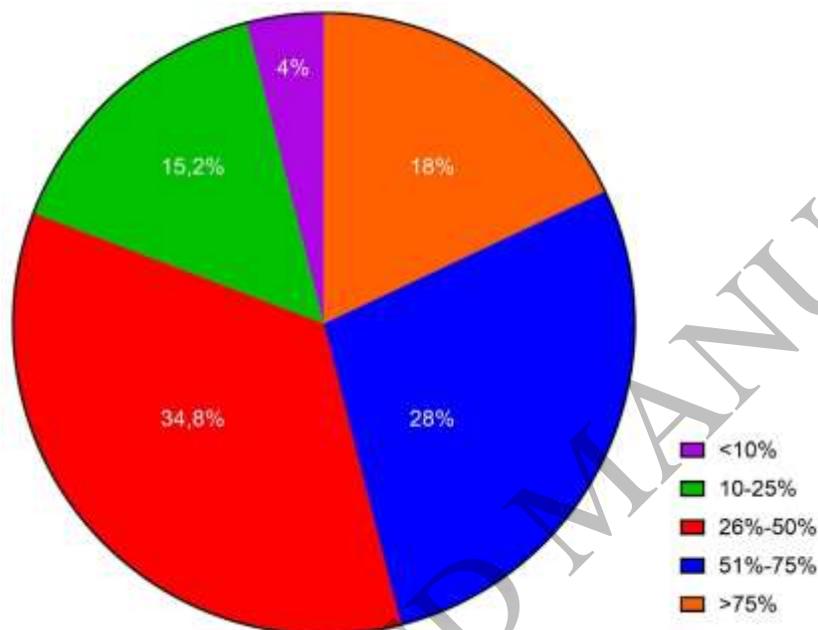
4 **Figure 4b. The proposed “optimal” components of the HF-specific SPC.**



5

1 Figure 5. **The anticipated use of the polypill. Estimated proportion of HF<sub>r</sub>EF patients who**  
 2 **could be offered an HF-specific SPC.**

3 Responses to the question: *“To what percentage of your HF<sub>r</sub>EF patients would you offer the*  
 4 *polypill?”*



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7 Figure 6. **Patient’s perspective on single-pill combination.**

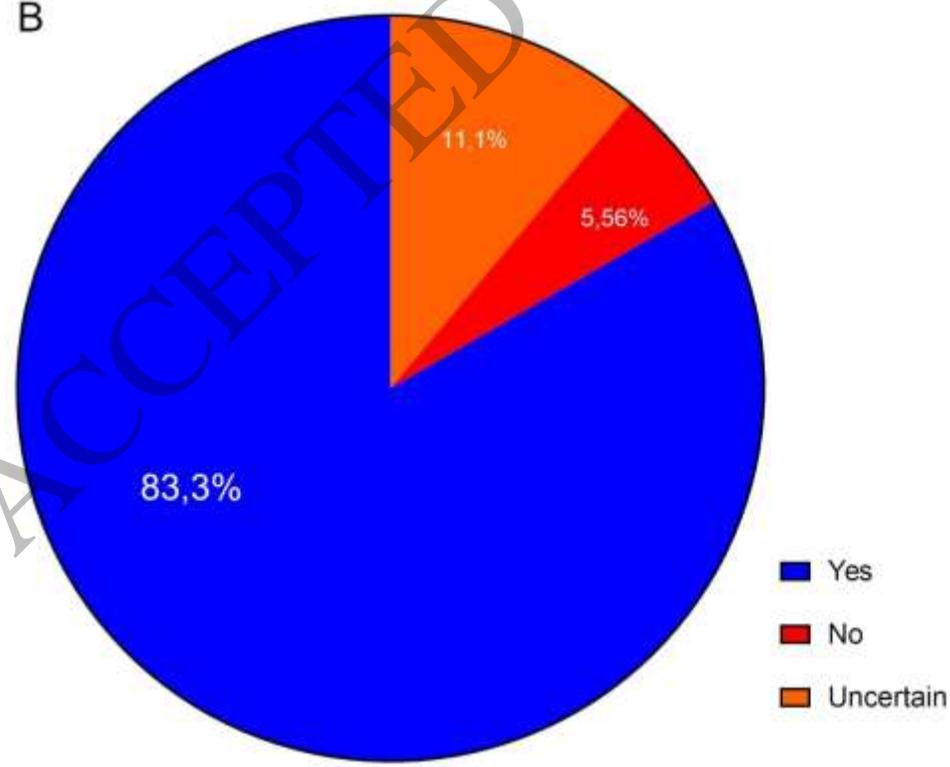
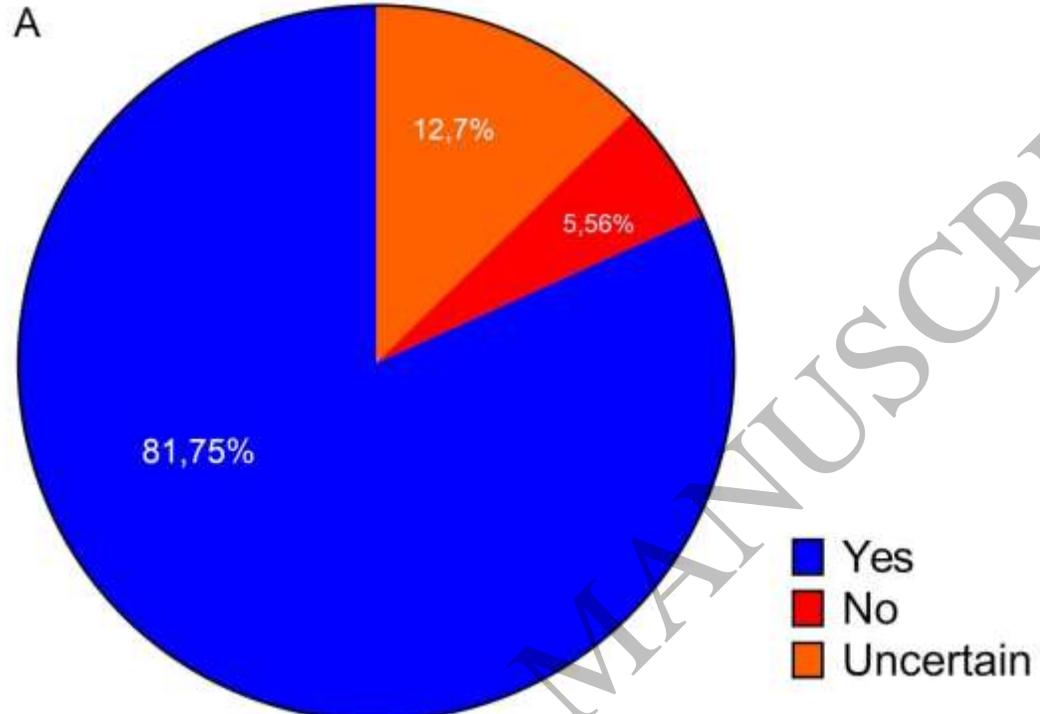
8 Figure 6a. **Patient interest in reducing pill burden through a single-pill solution.**

9 Responses to the question: *“Would you be interested in a solution that allows you to take fewer*  
 10 *pills per day (e.g. one tablet containing several medications)?”*

11 Figure 6b. **Patient willingness to switch to an HF-specific SPC if cost-neutral.**

12 Responses to the question: *“If your doctor offered to replace several of your current medications*

1 with a single pill containing the same substances (a so-called polypill), would you agree if it did  
2 not involve any additional cost?"



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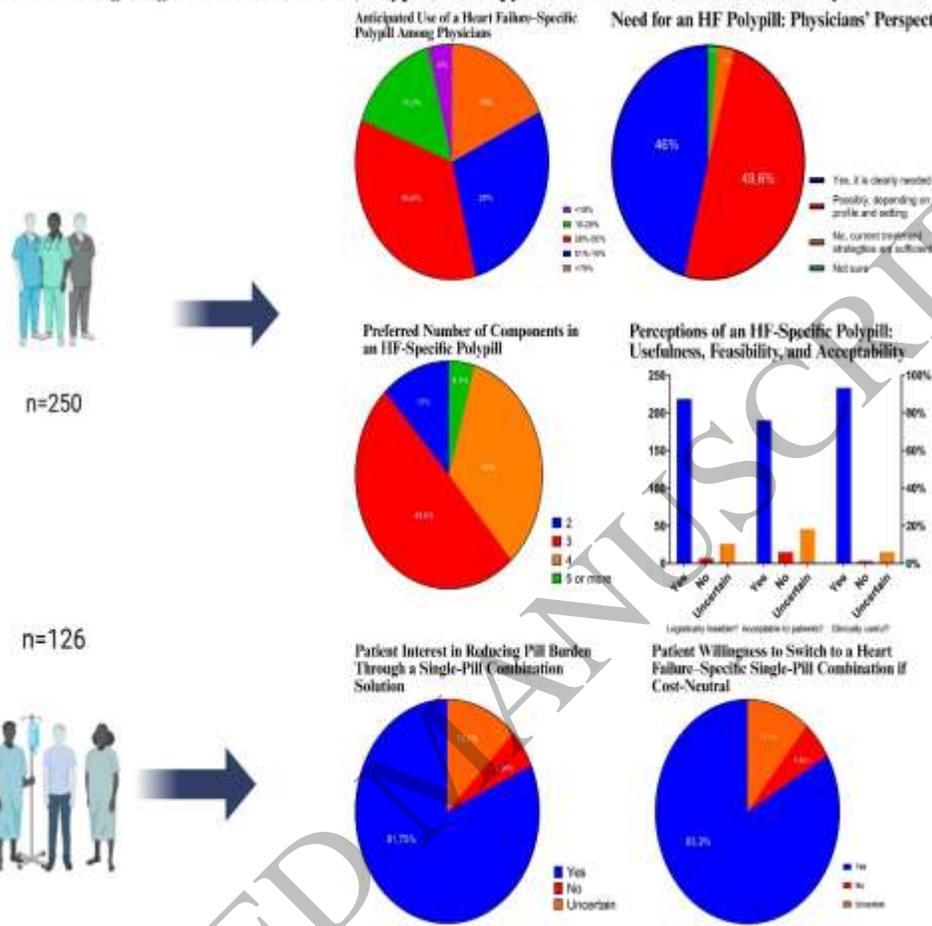
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*Attitudes Toward Using Single-Pill Combination (Polypill) Therapy in Heart Failure: Patients' and Physicians' Perspectives*



Graphical Abstract  
297x210 mm (x DPI)

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