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Results of an international crowdsourcing survey on the treatment of non-ST segment elevation ACS patients at high-bleeding risk undergoing percutaneous intervention

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ABSTRACT

Aims: Choosing an antiplatelet strategy in patients with non-ST segment elevation acute coronary syndrome (NSTE-ACS) at high bleeding risk (HBR), undergoing post-percutaneous coronary intervention (PCI), is complex. We used a unique open-source approach (crowdsourcing) to document if practices varied across a small, global cross-section of antiplatelet prescribers in the post-PCI setting.

Methods and results: Five-hundred and fifty-nine professionals from 70 countries (the 'crowd') completed questionnaires containing single- or multi-option and free form questions regarding antiplatelet clinical practice in post-PCI NSTE-ACS patients at HBR. A threshold of 75% defined 'agreement'. There was strong agreement favouring monotherapy with either aspirin or a $P2Y_{12}$ inhibitor following initial DAPT, within the first year (94%). No agreement was reached on the optimal duration of DAPT or choice of monotherapy: responses were in equipoise for shorter (≤3 months, 51%) or longer (≥6 months, 46%) duration, and monotherapy choice (45% aspirin; 53% $P2Y_{12}$ inhibitor). Most respondents stated use of guideline-directed tools to assess risk, although clinical judgement was preferred by 32% for assessing bleeding risk and by 46% for thrombotic risk.

Conclusion: The crowdsourcing methodology showed potential as a tool to assess current practice and variation on a global scale and to achieve a broad demographic representation. These preliminary results indicate a high degree of variation with respect to duration of DAPT, monotherapy drug of choice following DAPT and how

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thrombotic and bleeding risk are assessed. Further investigations should concentrate on interrogating practice variation between key demographic groups.

1. Introduction

In patients with non-ST segment elevation acute coronary syndrome (NSTE-ACS) at high bleeding risk (HBR), current guidelines recommend short duration of dual antiplatelet therapy (DAPT) with aspirin (ASA) and the $P2Y_{12}$ inhibitor clopidogrel, followed by monotherapy with ASA thereafter, in the post percutaneous coronary intervention (PCI) setting [1,2]. Randomised data from the CAPRIE trial, however, show that clopidogrel monotherapy reduces hospitalisation for gastrointestinal bleeding compared with ASA 325 mg daily, and that gastrointestinal bleeding is the most prevalent bleeding occurrence after PCI in the outpatient setting [3]. In addition, since the publication of the most recent set of guidelines (ESC in 2020), at least two independent meta-analyses suggest that discontinuing ASA and continuing $P2Y_{12}$ inhibitor monotherapy after short duration DAPT, provides additional protection against bleeding, without increasing thrombotic risk [4,5]. The choice of antiplatelet strategy in the HBR population is therefore complicated and despite growing evidence supporting the use of $P2Y_{12}$ monotherapy following initial DAPT [4–11], it is reasonable to expect that practice may vary.

To gain insight into current practices and variation with respect to antiplatelet therapy, we solicited input from a global audience of cardiology professionals. Given the inherent selectivity of more traditional survey methods, where participants are often predetermined, we utilised an open-source approach, driven primarily through social media. This novel 'crowdsourcing' methodology was chosen for its potential to reach a broad audience of antiplatelet prescribers. Here, we describe the findings of this preliminary study with respect to adherence to guideline-directed care in NSTE-ACS patients at HBR, post-PCI, from a small, global cohort of professionals.

2. Methods

The International Society of Cardiovascular Pharmacotherapy (ISCP) and Radcliffe Medical Education developed a project to assess current clinical practices in different World regions regarding the treatment of NSTE-ACS patients at HBR, post-PCI. To this end we appointed an expert Steering Committee (SC) to preside over:

i) the desired characteristics of the crowd;
ii) the design of the questions;
iii) the interpretation of the results.

2.1. Selection of steering committee members and the crowd

Fifteen SC members were invited to take part, based on their expertise in the treatment of ACS and their contribution to medical literature in this field. The following criteria were established to identify potential SC members: known expertise in ACS patient management, PCI and use of antiplatelet agents; >5 years' experience managing high volume ACS patients; contribution to ACS and antithrombotic literature (at least one co-authorship in a top-tier journal on the subject), and/or input into national or international clinical guidelines. Final selection was made based on the willingness to take part in the creation of the survey and the resulting publication.

2.2. Crowd characteristics

The selection process was designed to achieve representation across geographies, practice seniority, nature of primary practice, specialty and sex. Prerequisite experience in prescribing antiplatelet therapy and familiarity with the topic was required to provide informed insight.

In line with the above, the SC provided the following guidance for selecting individuals to take part:

Obligatory criteria

- Currently managing ACS patients
- Be a knowledgeable prescriber of antiplatelet therapy
- Be deemed to have a sound understanding of ACS/antiplatelet treatment literature

Desirable criteria

- Be experienced in PCI procedures and post-PCI management
- Have involvement in clinical trials for antiplatelet therapy or related therapy areas
- Be a local clinical decision maker/clinical policy shaper
- Be regarded as a key opinion leader in this field

Demographic questions were used to screen candidates for eligibility (see 'Crowd registration' for more detail); registrants were granted access to the crowdsourcing platform if they satisfied the first two clauses of the above obligatory criteria as a minimum; other criteria (seniority, geography, nature of primary practice) were used to estimate how broad participation was.

2.3. Crowd recruitment

The crowd was recruited to take part both directly (through direct email) and indirectly (through social media channels).

2.3.1. Direct recruitment

Contributions were sought from those who met the defined criteria, directly by members of the SC and representatives of the ISCP. The ISCP is represented by an executive committee and board of directors, representing countries from each major continent. Therefore, ISCP members were encouraged to promote the project directly to known professionals from their region.

In addition, Radcliffe Medical Education sent direct emails (total 269) to relevant participants from Radcliffe Cardiology's global database of health care professionals (HCPs); this approach was used as a secondary tool to recruit from geographic regions where the SC or ISCP members had no or low traction. Members of the editorial boards of the Interventional Cardiology Review and European Cardiology Review journals (both owned by Radcliffe Cardiology) were also invited to identify suitable crowd members (total 131 emails sent). Members of the SC and the ISCP with social media profiles were encouraged to actively promote posts to their followers [12].

2.4. Crowd registration

See **supplementary materials, S1** for details of the registration process and demographic questions used for eligibility screening.

2.5. Sample size and representation

No upper limit was defined in line with the overall ambition of capturing the prevailing insight and practices from a crowd representative of a wide range of geographies and experience.

2.6. Data collection and statistical analysis

Participants answered questions housed on the crowdsourcing platform, accessible via Google Chrome browser. Data analysis was performed blinded to the respondents' demographics. Questions were of three types:

i. Radio buttons or drop down for single option questions
ii. Multiple choice checkboxes for multi-selection questions
iii. Free form, where the respondents could type their answer.

For free form questions, all answers were combined into one for simultaneous review without statistical analysis. These were therefore analysed manually. For the remaining two types of questions, the server computed the top voted answer, frequency of each chosen solution and if the answer was a number, it computed: count, mean, standard deviation (SD), min, 25%, 50%, 75% and max.

To see the questions, see **supplementary materials, S2**.

Features from the HyperText Markup Language (HTML) source, as well as other raw data attributes, were extracted to perform quantitative analyses on the responses.

In line with general accepted practice, a threshold of 75% was defined as consensus on all single option questions [13].

3. Results

3.1. Crowd demographics

A total of 840 individuals registered to participate in the program, 559 of whom proceeded to complete the survey. Names and affiliations of all collaborators are listed in **Supplementary materials, S3**. Among registrants, five were rejected for failure to fulfil the eligibility criteria. Completed surveys were submitted from individuals representing six geographical regions and from across 70 countries. Country representation varied (range 1–47; **Supplementary material, S4**). The experience of respondents was measured by the number of reported ACS patients treated/year with 13% reporting <50, 34% 50–200, 34% 200–500 and 19% >500. Among the individuals who completed the survey, 52% identified themselves as interventional cardiologists, 42% as general cardiologists, 3% as other prescriber and 3% as 'Other' (catheter laboratory director, Coronary Care Unit cardiologist, general physician/doctor, head of cardiac and vascular surgery, intensive care specialist); 64% of responders reported more than 10 years' experience in practice and 59% working in a university/teaching hospital (**Supplementary materials, S5**). All respondents met the criteria of antiplatelet therapy prescriber.

3.2. Ideal and current practice

Respondents were initially asked about their ideal practice, irrespective of barriers to treatment such as access or reimbursement, local operating procedures or recommendations from international or local guidelines. Five-hundred and twenty-five (94%) respondents were in favour of monotherapy following an initial period of DAPT in patients assessed to be at HBR following PCI (Fig. 1A). In those who agreed with the use of monotherapy in this context (monotherapy advocates), the majority ($n = 328$, 72%) selected monotherapy use for longer than 12 months (Fig. 1B). Monotherapy advocates' preferred agent was split roughly equally between ASA ($n = 212$, 45%) and a $P2Y_{12}$ inhibitor ($n = 250$, 53%). Respondents' choice of $P2Y_{12}$ inhibitor as their ideal monotherapy agent was further split as follows: 127 (27%) clopidogrel; 104 (22%) ticagrelor; 19 (4%) prasugrel (Fig. 2A). Regional variation displayed generally the same equipoise for ASA vs $P2Y_{12}$ receptor inhibitor as observed at the global level, and across the experience level of respondents (namely, length of time post-qualification [<5 years; 5–10 years; >10 years]).

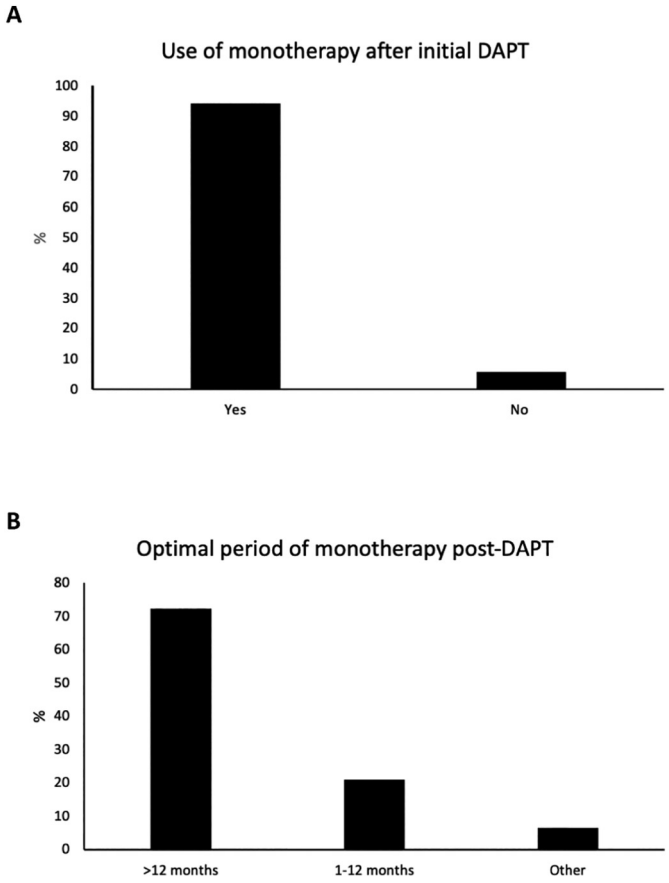

Fig. 1. Optimal monotherapy use after initial period of DAPT in NSTE-ACS patients at HBR: Respondents were asked whether they (A) agreed with the use of monotherapy following an initial period of DAPT (Yes, 94%; No, 6%), and (B) for those who agreed with the use of monotherapy, what they felt the optimal duration of monotherapy was after initial duration of DAPT (>12 months, 72%; 1–12 months, 22%; Other, 6%).

Monotherapy advocates did not agree on an optimal period of DAPT following PCI, although 3 months ($n = 204$, 39%) was the most frequently selected option (12 months [$n = 115$, 22%]; 6 months [$n = 94$, 18%]; 1 month [$n = 63$, 12%]; >12 months [$n = 31$, 6%]; other [$n = 16$, 3%]), (Fig. 2B). Stated differently, 51% opted for ≤3 months, and 49% opted for ≥6 months DAPT duration.

The second section of the survey asked about current practices and empirical use of guidelines. Of all respondents, 486 (87%) confirmed that they carry out the approach that they had advocated as their perceived ideal practice.

3.3. Influences on current practice

Respondents were asked to select the factors that influenced their antiplatelet preferences, including published guidelines and randomised controlled trials. Respondents were asked to make multiple selections from a list identified by the SC that were relevant to their decision-making. The ESC and ACC/AHA guidelines were the most highly selected ($n = 306$, 61% and $n = 166$, 33%, respectively) [1,2]. This was followed by TWILIGHT ($n = 121$, 24%), STOP-DAPT 2 ($n = 111$, 22%) and GLOBAL LEADERS ($n = 106$, 21%) trials [6,7,14]. Other influential literature cited included the Japanese Circulation Society guidance (n = 30, 6%) and the Brazilian Society of Cardiology guidelines (n = 10, 2%).

Respondents were asked to rank factors impacting their choice of $P2Y_{12}$ inhibitor on a Likert scale (scale 1–5: 1, least influential; 5, most influential). RCT evidence of safety was the most influential factor

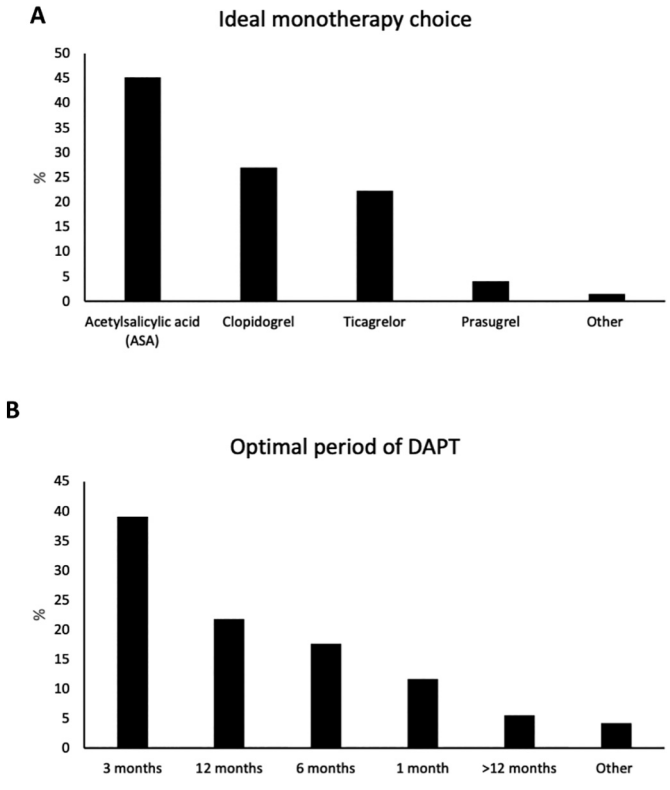

Fig. 2. Optimal monotherapy choice in DAPT duration in NSTE-ACS patients at HBR: Respondents were asked to select (A) ideal monotherapy choice irrespective of any current barriers to access (ASA, 46%; clopidogrel, 26%; ticagrelor, 22%; prasugrel, 4%; Other, 2%); (B) optimal period of DAPT (3 months, 39%; 12 months, 22%; 6 months, 18%; 1 month, 11%; >12 months, 5%; Other, 2%).

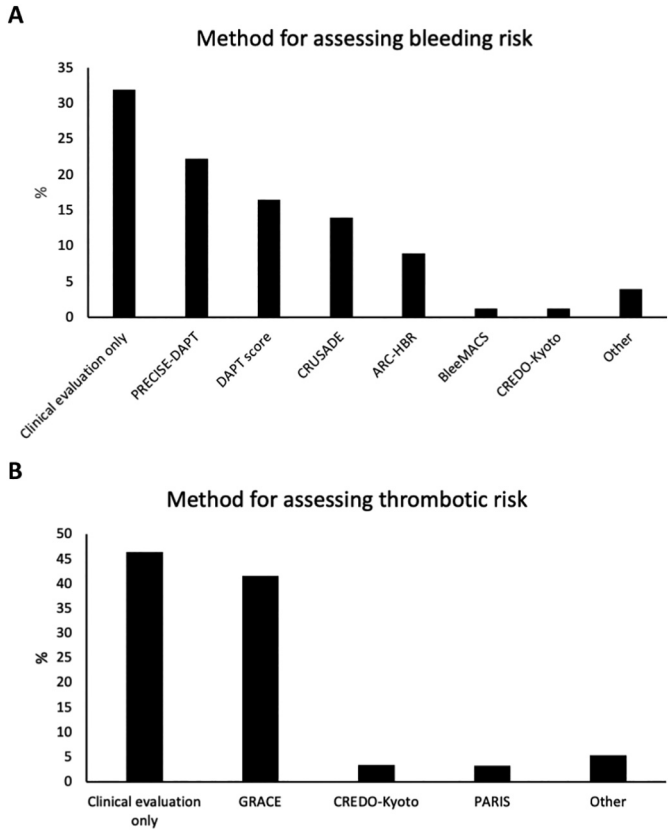

Fig. 3. Bleeding and thrombotic risk assessment practices: Respondents were asked which method they most frequently used for assessing (A) bleeding risk and (B) thrombotic risk in NSTE-ACS patients following PCI.

(mean score 4.6 [SD 0.6]), followed by RCT evidence of efficacy, bleeding risk, thrombotic risk and patient related factors (all mean score 4.4 [SD 0.7]). This was followed by guideline recommendations (mean 4.2 [SD 0.7]), and then compliance with local protocols (mean 3.6 [SD 1.0]). The least influential factor was cost/availability (mean 3.5 [SD 1.2]).

Clinical judgement over any single standardised score was the most common way to assess bleeding and thrombotic risk ($n = 178$ [32%] and $n = 256$ [46%], respectively, Fig. 3). Among the risk scores, PRECISE-DAPT was the method most commonly used by respondents to measure bleeding risk ($n = 122$, 22%). This was followed by DAPT score ($n = 89$, 16%), CRUSADE ($n = 78$, 14%), and ARC-HBR ($n = 50$, 9%).

When asked to what extent their routine practice aligns with that of the two major international guidelines on NSTE-ACS, 324 (58%) respondents said their clinical practice 'often' followed ESC guidelines (the remaining stated 'always' $n = 61$, 11%; 'sometimes' $n = 139$, 25%; 'rarely' $n = 28$, 5%; 'never' n = 6, 1%; Fig. 4A). Two-hundred and forty (43%) respondents said their clinical practice 'often' followed ACC/AHA guidelines (the remaining stated 'always' $n = 45$, 8%; 'sometimes' n = 178, 32%; 'rarely' $n = 72$, 13%; 'never' $n = 22$, 4%; Fig. 4B).

4. Discussion

4.1. Crowdsourcing methodology

To our knowledge, this is the first use of a crowdsourcing methodology to assess practices with respect to antiplatelet therapy in NSTE-ACS. It provides insight in an era where management of patients after ACS is becoming increasingly complex, not least because of the rapidly advancing field of antithrombotic treatment and the lack of strong (class I) guidance from guideline documents regarding the specific challenges that HBR patients present to practitioners [1,2]. We document current practices from a global 'crowd' of practicing physicians, to derive insight on the treatment of NSTE-ACS patients at HBR undergoing PCI.

Compared with a traditional prospective survey, where respondents are typically identified in advance and their participation solicited, this methodology provides a more democratic approach and thus a broad view of current practices. Our respondents included practitioners from six continents, 70 countries and represented a broad spectrum of experience and institution type (see **Supplementary materials, S5**). We believe this methodology, with its wide-ranging demographic uptake, is a valuable tool, given its ability to rapidly map the degree of consensus or controversy on clinically complex questions across the globe.

4.2. Use of monotherapy and determining duration of DAPT

With respect to the use of monotherapy after an initial period of DAPT in individuals at HBR, there was agreement on the use of monotherapy within 12 months, with most respondents favouring a duration beyond 12 months. The crowd, however, did not agree on optimal duration of DAPT, although most (51%) did agree with treating for 1–3 months (aligning with current ESC recommendations) [1]; there was also substantial support for 12 months DAPT (perhaps reflecting a class IIb, level of evidence C recommendation from the ACC/AHA guidelines, albeit with no reference to HBR) [2]. This variation in practice is not entirely surprising given that neither the ESC nor the ACC/AHA guidelines provide class I recommendations in HBR patients, leaving practitioners to determine DAPT duration based on their own estimation of bleeding and thrombotic risk. Thus, determining risk is a critical step in deciding the duration and choice of DAPT.

It is noteworthy that the European guidelines recommend PRECISE-DAPT or ARC-HBR criteria to estimate bleeding risk [15–17]. Interestingly, our results indicate that ARC-HBR was used by only 9% of

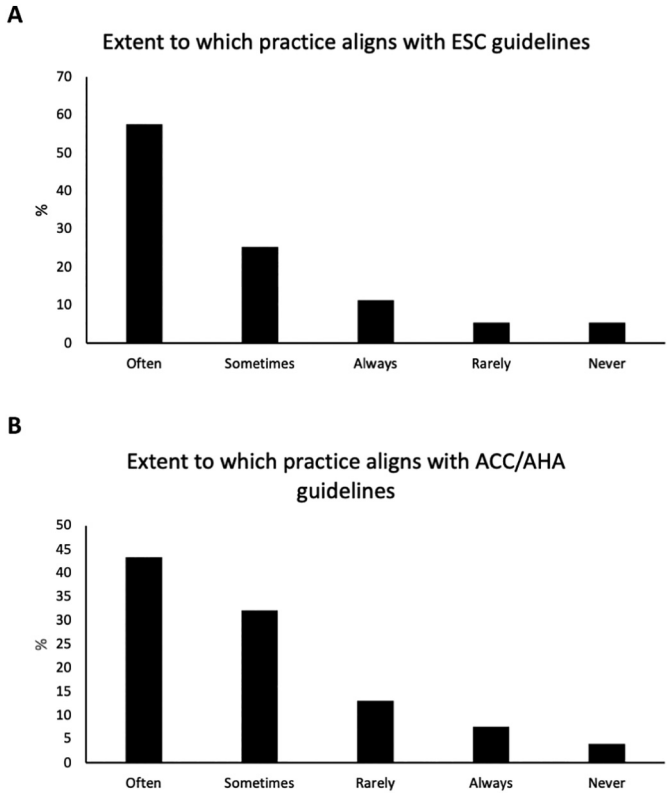

Fig. 4. Routine practice alignment with clinical practice guidelines: Respondents were asked how often their routine practice, with respect to the use of antiplatelet therapy in NSTE-ACS patients at HBR post-PCI, aligned with (A) current ESC recommendations and (B) ACC/AHA recommendations.

respondents, possibly reflecting hesitancy to use a dichotomous scoring approach or the relative novelty of this system. A standout observation in our data was the degree to which respondents did not use the recommended bleeding or thrombotic risk assessments – clinical judgement being used preferentially (Fig. 3). This approach may reflect the diversity of bleeding and thrombotic risk scores and the lack of a universal, validated tool. Of note, practice varied considerably in relation to guideline documents (Fig. 4).

4.3. Monotherapy choice and impact of clinical guidelines

Our findings also showed variation with respect to monotherapy choice. Overall, respondents were equally likely to choose ASA or a $P2Y_{12}$ inhibitor. Interestingly, this equipoise may reflect the coexistence of two similar ECS 2020 guideline recommendations for either $P2Y_{12}$ inhibitor discontinuation (IIa B) or ASA discontinuation (IIa A) [1]. ASA, however, was the single most used antiplatelet agent overall.

In the 2020 ESC guidelines, several recent publications are considered in making the recommendation for shortening DAPT to 1–3 months [6,8,10,14]. The guidelines considered these study populations to be low bleeding risk and low-to-intermediate ischaemic risk; for them, a class I recommendation was made for the use of ticagrelor monotherapy in low bleeding risk patients after 3 months DAPT, on the basis of TWILIGHT [6]. In actual fact, the TWILIGHT study patients were designated as either HBR or high ischaemic risk; this was defined as the presence of at least one additional clinical feature and one angiographic feature (see Table 1 for study design details). However, the TWILIGHT cohort was not considered HBR in the ESC guidelines, in part, owing to the one-year BARC 3 or 5 bleeding rates being below the 4% cut-off (as defined in recent ARC-HBR criteria) [16] in both monotherapy and DAPT arms. Thus, according to the 2020 ESC guidelines, in high or very high bleeding risk patients, monotherapy after 1–3 month DAPT is either via ASA or clopidogrel (class IIa for either options as per guideline Fig. 7) [1]. Interestingly, monotherapy with clopidogrel or ticagrelor after 3–6 month DAPT is recommended with equal strength (class IIa) "…depending on the balance between the ischaemic and bleeding risk" (as per ESC guideline table entitled *Recommendations for post-interventional and maintenance treatment in patients with non-ST-segment elevation acute coronary syndrome*) [1].

Since the publication of the 2020 ESC guidelines, there has been growing support for the continuation of $P2Y_{12}$ receptor inhibitors as monotherapy in HBR patients [4,5,18]. The only large RCT evaluating a potent $P2Y_{12}$ inhibitor as monotherapy in a global population that included some patients at HBR is TWILIGHT [6]. STOPDAPT-2 included a share of HBR patients, but most were at low to intermediate thrombotic and bleeding risk, so the overall significantly lower cardiovascular and bleeding event rate with $P2Y_{12}$ monotherapy compared with DAPT cannot be extrapolated to entirely HBR populations [7] (see Table 1 for a comparison of ACS trials with short and long-term DAPT arms). Overall, recent meta-analyses and RCT data indicate that $P2Y_{12}$ inhibitor monotherapy offers safety advantages over DAPT [4–6] and older data indicate some ischaemic benefit of a P2Y12 inhibitor over ASA alone [3,19]. Currently, there is a lack of prospective head-to-head monotherapy comparison in HBR patients (as judged by universally adopted criteria) to recommend a specific antiplatelet agent over another. Hence, for now, practicing clinicians should be guided by the strongest randomised data, as well as guidelines. The strength of current randomised data supports use of a potent $P2Y_{12}$ inhibitor as monotherapy, after 3 months of DAPT in HBR patients undergoing PCI.

5. Limitations

This study had some limitations. First, the social media-driven recruitment means that the true denominator was unknown, therefore, the generalisability of the findings remains uncertain. Second, given the open-source design of the survey, we were unable to control for over- and under-representation from key demographic groups. Third, a true representative sample was not reached for Africa or Oceania (eight and seven respondents, respectively); therefore, these areas were excluded from regional assessments – but all regions and all countries were included in the overall analyses. Fourth, although social media was used for data acquisition, a substantial proportion of responses was derived from direct recruitment from the expert Steering Committee, members of the International Society of Cardiovascular Pharmacotherapy and from Radcliffe Cardiology via their database. As such, the true value of social media as a recruitment driver cannot be definitively measured in this sample. Fifth, because the overall number of completions were small (relative to the total global community of cardiologists and other antiplatelet prescribers in ACS), we cannot take this as conclusive evidence that the observed results are generalisable globally and therefore, we are unable to draw meaningful conclusions across different demographic or regional groups.

6. Conclusion

Crowdsourcing is a novel, open-source approach that has potential to capture practices from a broad demographic. In the present study, we used a combination of direct email and social media to drive registrations, highlighting its potential as an accessible and easily executable alternative to more traditional survey approaches, which rely on identifying the participant base. The wide reach afforded by crowdsourcing shows potential in providing democratic and agile mapping of crucial clinical practice scenarios.

In this preliminary study, our chosen methodology highlighted a high degree of variation with respect to the duration of DAPT, choice of monotherapy and how bleeding and thrombotic risk are determined, among a relatively small sample of cardiology professionals. Our results

Table 1
Summary of main trials in ACS comparing shorter duration DAPT (1–3 months) with longer term DAPT.

	Twilight	TICO	Global leaders	STOPDAPT-2	Smart-choice
$P2Y_{12}$ inhibitor	T	T	T	C	All (C, P, T)
Trial design	***n* = 7119** 12 months: Open label, randomised: Mono (T) vs DAPT	***n* = 3056** 12 months: Open label, randomised: Mono (T) vs DAPT	***n* > 16,000** 24 months: Open label, randomised: Mono T 23 months vs DAPT (C/T) 12 months, then ASA mono 12 months (C only in SIHD with elective PCI)	***n* = 3045** 12 months: Open label, randomised: Mono (C) vs DAPT	***n* = 2993** 12 months: Open label, randomised: Mono vs DAPT C: 76.9–77.6%; T/P: 22.4–23.1%
Outcomes and results					
Primary	Bleeding (BARC 2, 3, 5): **Superior in mono-T arm (incl. stable and acute sub-groups)**	Composite major bleeding and adverse cardiac and cerebrovascular events (death, myocardial infarction, stent thrombosis, stroke, or target-vessel revascularization): **Superior in mono-T arm (incl. All ACS sub-groups).**	Composite all-cause mortality or nonfatal MI: **Non-significant across SIHD and ACS groups**	Composite CV death, MI, stroke, stent thrombosis or TIMI major/minor bleed: **Superior in mono-C arm (non-significant in ACS sub-group)**	Composite all-cause death, myocardial infarction, or stroke: **Non-inferior in Mono arm**
Secondary	Death from any cause, nonfatal MI/stroke: **Non-inferior in mono-T arm** BARC 3 or 5 bleeding; TIMI major or minor bleeding; GUSTO moderate, severe, or life-threatening bleeding; ISTH major bleeding: **Superior in mono-T arm**	Major bleeding and major adverse cardiac and cerebrovascular events: **8 of 10 endpoints had no significant difference; major bleeding significantly lower in mono-T arm.**	Bleeding (BARC3/5): **Non-significant**	Composite thrombotic endpoint: **Non-inferior in mono-C arm** TIMI major/minor bleed: **Superior in mono-C arm**	Individual components of the primary composite end point: **Non-significant** BARC 2–5: **Significantly lower with mono (non-significant in the C sub-group)**
PCI indication					
All PCI			Y (SIHD or ACS)	Y (SIHD or ACS)	Y (SIHD or ACS)
All ACS (NSTEMI, unstable angina, STEMI)		Y (incl. 36% STEMI)			
NSTE-ACS only (NSTEMIS/unstable angina)					
NSTE-ACS + stable angina	Y				
Risk stratification					
Bleeding risk: Very high					
Bleeding risk: High	Y: ≥ 1 additional clinical feature and one angiographic feature associated with a high risk of ischemic or bleeding events (PRECISE-DAPT/PARIS)			Y: PARIS (19.3–20.1%); CREDO (7.1–7.4%)	
Bleeding risk: Medium				Y: PARIS (50.5–53.1%); CREDO (26.5–26.6%)	
Bleeding risk: Low		Y: without increased risk of bleeding	Y: no known overt major bleeding, history intracranial haemorrhage, stroke within previous 30 days	Y: PARIS (27.6–29.4%); CREDO (66–66.4%)	Y
Thrombotic risk: High	Y			Y: PARIS (14.1–14.3%); CREDO (7.5–8.1)	Low
Thrombotic risk: Medium				Y: PARIS (35.5–37.3%); CREDO (21.2–23.7%)	
Thrombotic risk: Low				Y: PARIS (48.6–50.2%); CREDO (68.2–71.3)	
Stent type					
DES	Y	Y	Y	Y	Y
BMS/other					
Treatment duration post-PCI					
1 month DAPT			Y	Y	
3 months DAPT	Y	Y			Y
Comparative period (mono vs DAPT)	9 months	9 months	23 months (T or C)	9	9
Other differences					
Ethnicity	N America, Europe, Asia	S Korea	WW (18 countries)	Japan	Korea
Key exclusion criteria	STEMI, cardiogenic shock, ongoing long-term treatment with oral anticoagulants, contraindication	Increased risk of bleeding, anaemia, thrombocytopenia	Known overt major bleeding, history intracranial haemorrhage, stroke within previous 30 days		Hemodynamic instability or cardiogenic shock; active pathologic bleeding, including gastrointestinal or genitourinary bleeding

Table 1 (*continued*)

	Twilight	TICO	Global leaders	STOPDAPT-2	Smart-choice
Bleeding criteria	Primary: BARC 2–5; secondary: TIMI, GUSTO, ISTH, BARC 3/5	TIMI	BARC	GUSTO	BARC

ACS, acute coronary syndrome; BARC, Bleeding Academic Research Consortium; BMS, bare metal stent; C, clopidogrel; CREDO-Kyoto, Coronary Revascularization Demonstrating Outcome Study in Kyoto; DAPT, dual antiplatelet therapy; DES, drug-eluting stent; GUSTO, Global Utilization of Streptokinase and TPA for Occluded arteries; ISTH, International Society on Thrombosis and Haemostasis; MI, myocardial infarction; Mono, monotherapy; P, prasugrel; PARIS, Patterns of Non-Adherence to Anti-Platelet Regimens in Stented Patients; PCI, percutaneous coronary intervention; PRECISE-DAPT, Predicting Bleeding Complications in Patients Undergoing Stent Implantation and Subsequent Dual Antiplatelet Therapy; SIHD, stable ischaemic heart disease; STEMI, ST-elevation myocardial infarction; T, ticagrelor; TIMI, Thrombolysis In Myocardial Infarction.

indicate that this sample embraced sources of literature outside of international guidelines and used their own clinical judgement to treat HBR patients. The use of antiplatelet therapy in HBR individuals is not only controversial, but merits careful consideration in future guidelines, given multiple unanswered clinical questions that currently preclude guidelines from forming class I recommendations.

As to how representative this present sample is of real-world practice remains to be determined; however, these largely hypothesis-generating results highlight important practices that warrant validation in larger studies. Subsequent studies on important participant subgroups are expected to yield a more detailed understanding on the sources of variation and may reveal interesting differences between key demographic groups according to speciality, experience level, and region of practice.

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