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The Fate of Patients Opportunistically Screened for Abdominal Aortic Aneurysms During Echocardiogram or Arterial Duplex Scans

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WHAT THIS PAPER ADDS

With a falling prevalence of abdominal aortic aneurysm (AAA) in the general population, opportunistic screening of high risk populations may become a more efficient approach than current population based screening programmes. There is a lack of contemporary data with long term outcomes evaluating this approach. This study demonstrates a high yield of AAA identification using opportunistic screening in patients attending hospital for transthoracic echocardiograms or lower limb arterial duplex scans. An evaluation of AAA diameter progression and clinical outcomes after an eight year follow up period demonstrated few of these AAAs were treated but those with an AAA were twice as likely to die during follow up.

Objective: To evaluate the long term outcomes of individuals who attended for transthoracic echocardiograms (TTEs) or lower limb arterial duplex scans (LLADS) and were opportunistically screened for abdominal aortic aneurysms (AAA).

Methods: Follow up of a prospective single centre pilot cohort study conducted between December 2012 and September 2014 at a tertiary vascular centre in the United Kingdom. Men and Women aged 65 and over were invited to undergo AAA screening when attending hospital for TTE or LLADS. Screening was performed by ultrasonographic examination of the abdomen at the end of their planned scans. AAA was defined as an abdominal aorta outer wall to outer wall anteroposterior diameter of 30 mm or more. Patients were excluded if they had a known AAA or previous abdominal aorta intervention. Follow up outcomes were evaluated in December 2020.

Results: 762 patients were enrolled in this study; 486 had TTE and 276 patients had LLADS. The overall incidence of AAA was 54 (7.1%) in the combined cohort, 25 (5.1%) in the TTE group, and 29 (10.5%) in the LLADS group. After a median 7.6 years, two of the 54 AAAs received intervention in the form of endovascular repair. Three others reached treatment threshold but were managed conservatively. The overall intervention rate was 3.7% of detected AAAs. Adjusted mortality rates in those with AAA *vs.* without was 64.8% and 36%, respectively (hazard ratio [HR] 2.02, $p < .001$). Diabetes (HR 1.35, $p = .015$) and older age (HR 1.18, $p = .17$) were the other factors associated with death.

Conclusion: AAA is associated with a significantly increased mortality rate. Populations attending hospital for TTE or LLADS demonstrate a higher prevalence of AAA than population based screening; however, the proportion offered AAA intervention was low. Further research into opportunistic screening should target those more likely to undergo AAA repair, unless other interventions are demonstrated, to reduce the general increased mortality in AAA patients.

Keywords: Abdominal aortic aneurysm, Mass screening, Peripheral arterial disease, Transthoracic echocardiography
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INTRODUCTION

Population based ultrasound screening for abdominal aortic aneurysm (AAA) in men is undertaken in numerous countries. Randomised controlled trials (RCTs) have demonstrated increased rates of AAA surgery and decreased rates of AAA rupture, which account for a significant reduction in the AAA specific mortality rate in screened patients.[1] Cost analyses in two RCTs demonstrated acceptable cost effectiveness of population screening in men.[2,3] RCTs of population screening in women have failed to demonstrate even a disease specific benefit, and subsequent analysis has shown they are unlikely to reach cost effectiveness even in very favourable conditions.[4]

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The National Health Service Abdominal Aortic Aneurysm Screening Programme (NHS AAASP) in the United Kingdom (UK) screens men over 65 and is largely based on protocols derived from the largest RCT, the Multicentre Aneurysm Screening Study (MASS), which demonstrated an AAA prevalence of 4.9%. In the year 2019 — 2020, the NHS AAASP scanned 222 182 men with only 0.9% having an AAA.[5] This incidence has slowly fallen since the programme's first report in 2015.[6] With a decreasing prevalence of AAA found on population screening in men and a lack of cost effectiveness in women, increased attention may be focused on the effectiveness of opportunistic or selective screening to reduce the overall AAA specific mortality rate.

AAAs are known to have a higher prevalence in patients with coronary artery disease and peripheral arterial disease (PAD), probably due to the shared risk factors.[7] Both these populations regularly have ultrasound based investigations and could have opportunistic screening for AAA at the same time for little additional cost. The risk of screening a population with established comorbidities is that it will increase the financial costs of AAA treatment and potentially decrease quality of life in individuals who have AAA diagnosed but are not suitable for treatment. This study reports the fate of individuals who had opportunistic screening for AAA as part of a feasibility study and discusses the utility of such screening.

MATERIALS AND METHODS

Setting and participants

A review of late outcomes was undertaken on a prospective single centre pilot cohort study conducted at a tertiary vascular centre in the UK. Between December 2012 and September 2014, male and female patients aged 65 and over who were undergoing transthoracic echocardiography (TTE) by an accredited clinical vascular scientist were invited to participate in the study. Those who agreed had an abdominal aortic measurement taken at the end of their TTE. Qualifying patients having a lower limb arterial duplex scan (LLADS) between January 2013 to August 2015 had their abdominal aortas scanned as part of this investigation and were included in the study. The indication for scan was not a factor determining eligibility. Patients in both groups were excluded on the basis of having had a previous abdominal aorta intervention or a known AAA. Consent was sought in all instances. The study received approval by an NHS research governance and ethics committee prior to commencement. It was undertaken prior to a routine requirement for trial registrations.

Outcome measures

An abdominal aorta outer wall to outer wall anteroposterior diameter measured using a transverse view of 30 mm or more was defined as an AAA. Those found to have an AAA from the screening were provided with information about the diagnosis and enrolled in the local AAA surveillance programme. The patient's age, sex, smoking status, family history of AAA, and comorbidities, which included hypertension, diabetes, and hypercholesterolaemia, were collected via a questionnaire administered at the time of their scan. Follow up outcomes were evaluated in December 2020. The central NHS spine was used to ascertain mortality status by evidence of a date of death on the patient's records. Vascular clinic appointment documentation and the results of repeat AAA scans were reviewed through the institution's electronic patient records.

Scanning protocol

AAA was assessed by an accredited clinical vascular scientist. Ultrasonographic examination of the abdomen was performed in the supine position at the end of their TTE or LLADS. B mode ultrasound in a transverse view starting from the epigastric region down to the abdominal aortic bifurcation was undertaken. Once the maximum abdominal aorta diameter was visualised, the image was frozen and a maximum anterior to posterior diameter was obtained using the outer edge of the anterior wall to the outer edge of the posterior wall (Fig. 1).

Statistical analysis

A presumption of non-normal distribution was made for all variables. Continuous variables are presented as median (interquartile range), and categorical variables as total numbers and percentages (%). Comparison between two groups was done using the Wilcoxon rank sum test. Multiple logistic regression analysis was used to assess for independent association with AAA. A p value of less than .05 was considered statistically significant. Adjusted survival analyses were conducted using a Cox proportional hazard model, using the whole study population as reference when required.

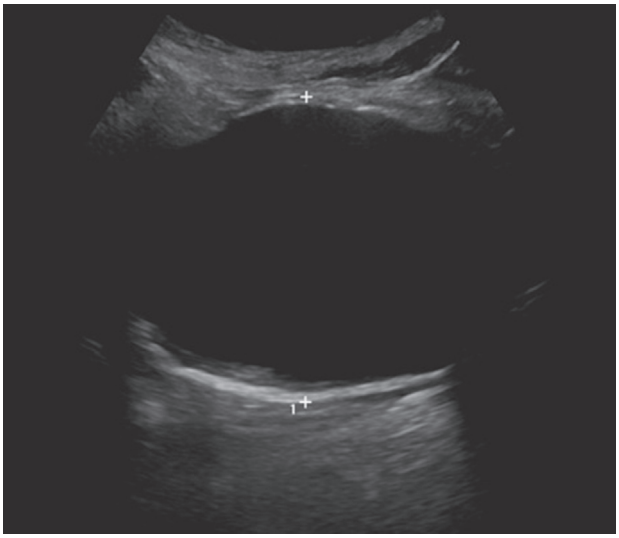

Figure 1. Transverse view B mode ultrasound image of abdominal aortic aneurysm, with white callipers demonstrating the outer wall to outer wall anteroposterior diameter measurement.

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Table 1. Baseline characteristics for patients screened for abdominal aortic aneurysms (AAAs) during transthoracic echocardiography, lower limb peripheral arterial duplex scans, and the combined group

	Transthoracic echocardiography (n = 486)	Lower limb peripheral arterial duplex scans (n = 276)	Combined population (n = 762)
Sex			
Male	316 (65.0)	172 (62.3)	488 (64.0)
Female	170 (35.0)	104 (37.7)	274 (36.0)
Age − y	76 (71–81)	77 (70–84)	77 (71–82)
Visit reason			
Valvular abnormality	160		
Coronary revascularisation	110		
Dysrhythmia or ECG abnormality	38		
Cardiac symptoms	33		
Acute coronary syndrome	28		
Ischaemic heart disease	26		
Heart failure	24		
Claudication		102	
Critical limb ischaemia		64	
Lower limb ulcer		38	
Acute limb ischaemia		34	
Diabetic foot		13	
Other	42	22	
Risk factors			
Hypertension	349 (71.8)	185 (67.0)	532 (69.8)
Current smoker	55 (11.3)	60 (21.7)	114 (15.0)
Ex-smoker	213 (43.8)	97 (35.1)	310 (40.7)
Pack years	20 (10–40)	30 (15–36)	24 (11–40)
Family history of AAA	6 (1.2)	2 (0.7)	8 (1.0)
Diabetes	121 (24.9)	112 (40.6)	233 (30.6)
Hypercholesterolaemia	327 (67.3)	186 (67.4)	512 (67.2)

Data are presented as n (%), or median (interquartile range).

RESULTS

A total of 486 patients (316 male, 170 female) and 276 patients (172 male, 104 female) underwent AAA screening during TTE and LLADS, respectively. They were followed up for a median duration of 7.6 years (7.1 — 7.8). Baseline demographic information can be found in Table 1. The overall incidence of AAA was 7.1% (Table 2). The median abdominal aortic diameter was 20 mm.

Transthoracic echocardiography cohort

A total of 486 patients were screened for AAA during TTE, the median age of the population was 76 (range 71 — 81). The majority of patients attended for evaluation of valvular function (33%) and pre-operative assessment for coronary revascularisation (23%). The abdominal aorta was not visualised in 11 patients (2.3%) and AAA was detected in 25 patients, a prevalence of 5.1%. Of these, 19 were male and six were female. The prevalence of AAA in this sample was 6.0% in men, and 3.5% in women (p = .36). Those with AAA were older than those without (p = .038) (Supplementary Table S1). The median AAA diameter was 33 mm (31 — 38) (Fig. 2A). The unadjusted mortality rate for those with AAA was 52% compared with 38% in those who did not have an AAA (p= .18).

Men vs. women with abdominal aortic aneurysm. The median AAA diameter was 36 mm (31 — 41) in women, and 33 mm (32 — 38) in men (p = .92). Women with an AAA had a median age of 83 (78 — 81), while men had a median age

Table 2. Characteristics of patients with identified abdominal aortic aneurysms after screening during transthoracic echocardiography (n = 486), lower limb peripheral arterial duplex scans (n = 276), or the combined group (n = 762)

	Transthoracic echocardiography	Lower limb peripheral arterial duplex scans	Combined population
Incidence	25 (5.1)	29 (10.5)	54 (7.1)
Men	19 (6.0)	19 (11.0)	38 (7.8)
Women	6 (3.5)	10 (9.6)	16 (5.8)
Age − y	79 (73–84)	77 (70–84)	78 (74–84)
Men	78 (69–88)	77 (72–84)	78 (72–84)
Women	83 (72–87)	81 (77–85)	83 (77–85)
Diameter − mm	33 (31–38)	36 (32–41)	35 (31–40)
Men	33 (32–38)	34 (31–38)	34 (31–38)
Women	36 (31–41)	41 (34–45)	40 (32–43)
Deceased	188 (38.7)	123 (44.6)	311 (40.8)
AAA	13 (52.0)	22 (75.9)	35 (64.8)
No AAA	168 (36.4)	87 (35.2)	255 (36.0)

Data are represented as n (%), or median (interquartile range).

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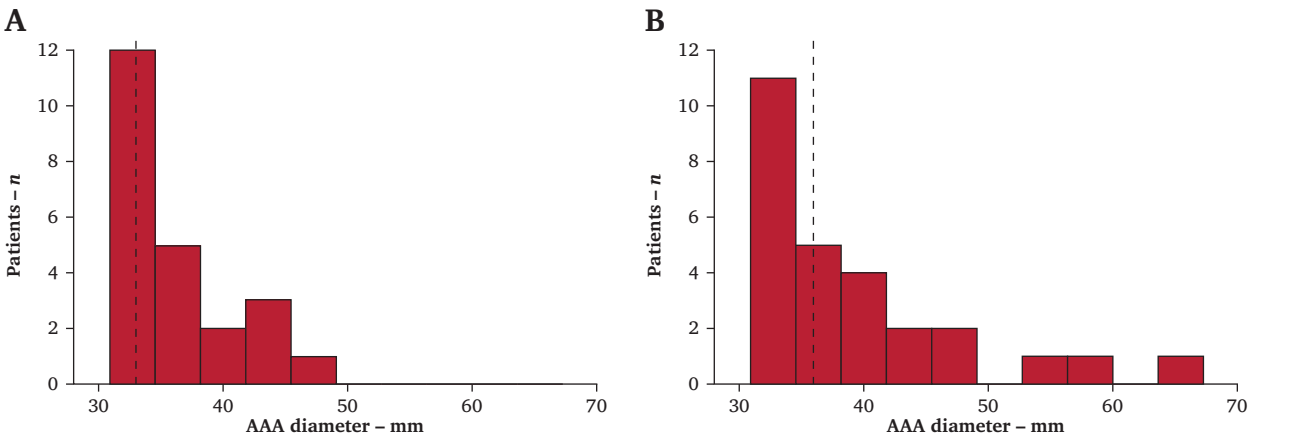

Figure 2. Distribution of abdominal aortic aneurysm (AAA) diameter identified in those screened during other ultrasound investigations. (A) AAA diameter distribution in transthoracic echocardiogram group. (B) AAA diameter distribution in lower limb arterial duplex scan group. The dotted lines represent the median values.

of 78 (73 — 84) ($p = .37$). Of the six women found to have AAAs, two reached the treatment threshold. One underwent an endovascular aneurysm repair (EVAR) four years after initial screening, and the other developed a 67 mm aneurysm six years after screening that was managed conservatively. Overall, five of the six women with AAA did not have any AAA intervention. All 19 men with AAA did not have any AAA intervention. One of them reached the treatment threshold with a 63 mm AAA after eight years; however, this was managed conservatively. Supplementary Table S2 lists all the patients identified as having an AAA during TTE and the most recent outcomes of their AAA surveillance.

Risk factor association. Hypertension, being an ex-smoker, and hypercholesterolaemia were the most common risk factors identified in the population screened during TTE. Multiple logistic regression analysis identified age ($p = .007$) and smoking pack years ($p < .001$) as independent risk factors for AAA (Supplementary Table S3).

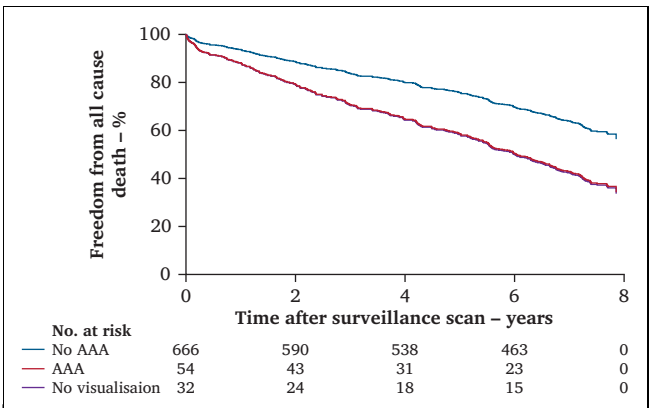

Figure 3. Cumulative Kaplan—Meier estimate of curves comparing those with abdominal aortic aneurysm (AAA), without AAA, and those with non-visualised abdominal aortas in the combined cohort of patients screened during transthoracic echocardiogram and lower limb arterial duplex scan.

Lower limb arterial duplex scan cohort

A total of 276 patients were screened for AAA during LLADS, the median age in this population was 77 (70 — 84) years (Table 1). The majority of patients attended due to claudication (37%) and features of chronic limb ischaemia (23%). The abdominal aorta was not visualised in 24 patients (8.7%), AAA was detected in 29 patients, a prevalence of 10.5% (Table 2). Of these, 19 were men and 10 were women. Male and female AAA prevalence was 11.0% and 9.6% respectively ($p = .21$). The median aortic diameter was 36 mm (32 — 41) (Fig. 2B). The unadjusted mortality rate in those with AAA was 76% compared with 35% without AAA ($p < .001$) (Supplementary Table S4).

Men vs. women. The median AAA diameter was 41 mm (34 — 45) in women and 34 mm (31 — 38) in men ($p = .046$). Women with an AAA had a median age of 81 (77 — 85), while men had a median age of 77 (72 — 84) ($p = .21$). Of the 10 women found to have AAAs, two reached treatment threshold. One had an AAA diameter of 40 mm at screening that grew to 55 mm 2.5 years later. The second had a 55 mm AAA during screening that grew to 59 mm three years later. None of the women with AAAs received intervention for their aneurysms. Of the 19 men with AAA, one received an EVAR, and one was found to have a 67 mm AAA during screening that was managed conservatively. Supplementary Table S5 lists all the patients with AAA identified during LLADS and the most recent outcomes of their AAA surveillance.

Risk factor association. Hypertension, hypercholesterolaemia, and diabetes were the most common risk factors identified in the population screened during LLADS. Multiple logistic regression analysis identified being a smoker ($p = .006$) as an independent risk factor for AAA (Supplementary Table S6).

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Mortality

The overall mortality rate in those with and without an AAA was 64.8% and 36.0%, respectively ($p < .001$). Figure 3 demonstrates the adjusted Kaplan–Meier curves for those with AAA, without AAA, and those with abdominal aortas that were not visualised. Death during follow up was independently associated with having an AAA (HR 2.02, $p < .001$), a non-visualised aorta (HR 1.96, $p = .004$), those who were older (HR 1.06 per year, $p < .001$), and having diabetes (HR 1.36, $p = .015$) (Supplementary Figure S1).

DISCUSSION

This study demonstrates a high yield of AAA identification using the approach of opportunistic screening of select high risk populations. At present, the European Society for Vascular Surgery recommends one off AAA screening for all men aged 65 years of age.[8] The American College of Cardiology/American Heart Association guidelines take the more targeted recommendation of screening men 65 years of age who have ever smoked.[9] There has been a dramatic decrease in the prevalence of AAA in the UK, from 4.7% in the last century, to 0.9% currently.[10] This has been mirrored in other Western populations.[11,12] Targeted screening of high risk populations is a potential cost effective alternative to the population based screening.

A 2018 meta-analysis of 20 observational studies with 43 341 participants demonstrated a prevalence of AAA in those attending for TTE of 3.3%; 4.6% in men, and 1.4% in women.[13] This study corroborated these findings with a prevalence of 5.5%. A prevalence of 3.5% in women is an almost four fold higher than that in population level screening of men in the UK.

Numerous studies have supported the positive correlation between the prevalence of PAD and AAA.[14,15] Despite this, there are limited studies implementing opportunistic screening for AAA in those who attend for LLADS. The most contemporary data are from Jones *et al.*, which evaluated various targeted screening strategies for AAA.[16] Within the group of patients who underwent ultrasound for suspected carotid artery atherosclerosis or PAD, AAA prevalence was found to be 6% in men and 2.2% in women. This study found a male and female prevalence of 11% and 9.6% respectively.

The increased rate of AAA found in populations attending for TTE or LLADS scans were irrespective of gender, and smoking history was the only consistent risk factor associated with AAA. Difference in prevalence may partially be attributed to the difference in imaging protocols. Gürtelschmid *et al.* demonstrated a difference in mean aortic diameter measurement of 4.1 mm between inter to inner and outer to outer measurements in a known AAA population with a mean aortic diameter of 42 mm.[17]

The feasibility of opportunistic screening is supported by the convenience of not requiring additional equipment and an acceptable abdominal aorta visualisation rate of 95.4%. While the time taken for AAA scanning was not measured in this study, previous reports have suggested a very small additional scan time of 31 seconds to under five minutes, and an 86% success rate for abdominal aorta visualisation.[13]

The clinical utility and cost effectiveness of implementing such a screening programme however depends on whether this high pick up rate translates to a meaningful impact on the patient's clinical course in the form of identifying large AAAs that are amenable to treatment and reducing the AAA mortality rate. Despite a higher AAA prevalence in the combined cohort than the landmark MASS study, the proportion which actually underwent surgical repair is smaller (4% and 3.4% in the TTE and LLADS cohorts, respectively). The MASS study demonstrated elective surgery rates as high as 40.2%.[1] Furthermore, 2% of total screened population of MASS received intervention for AAA, whereas 2.9% were found to have AAAs that were not for intervention. These contrast with the values observed in this study which showed that only 0.26% of those screened had an AAA that underwent intervention, whereas 6.8% had an AAA that was not for intervention. For one AAA that is amenable to surgery, this study found 26 AAAs that either did not grow in diameter to reach treatment threshold or for whom the risks of surgery outweighed the benefit or the patients declined subsequent surveillance.

While both the cohorts demonstrated a significantly higher mortality rate in those with AAA than those without, data sources for this post-study analysis preclude comment on what proportion of these were aneurysm related deaths. It appears unclear whether the risk benefit of an overall intervention rate of 3.7% as seen in this study is sufficient to justify this opportunistic screening approach. Although the benefit of screening in men has continued to be shown in meta-analysis, population based approaches do not seem to show benefit for women.[18,19] This study however presents a small amount of data that may potentially support targeted opportunistic screening of men and women within the subset of patients who are at higher risk of AAA and who are fit for repair. Targeted screening of those who attend for theses scans but with stable or non-critical comorbidities and a smoking history may offer a superior strategy.

Finally, these results demonstrated the significance of having an AAA as a poor prognostic marker in this contemporary cohort. The adjusted mortality rate of those with AAA was almost twice as high as those without. With half the AAA population in this study dead after just six years irrespective of management strategy, the relevance of the general debate on long term durability of interventional treatments of AAA may be becoming less important. Arguably AAA could be seen as a highly significant predictor of general mortality risk, even in the context of the very comorbid population of the study. Opportunistic and potentially population based AAA screening could have continued with much greater efficacy if they instigated and demonstrated benefit from aggressive risk factor modification. This looks to have the potential to dwarf the benefits of isolated treatment or surveillance of AAA pathology but is yet to be proven in a randomised setting.

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Limitations

This was a pilot study intended to inform a larger study of surveillance, as such it did not anticipate a need for long term follow up data regarding aneurysm related outcomes. At the time of initial analysis, its low rate of patients requiring repair made a larger study uneconomical. Thirteen of 54 patients diagnosed with an AAA declined subsequent surveillance. Despite all being ultrasound based investigations, the adjunct of AAA screening to a transthoracic echocardiogram may require additional training, as cardiac sonographers are not generally qualified in vascular ultrasound. Any future studies into opportunistic screening require a mechanism to collect late aneurysm related and all cause deaths to guide the recommendation for targeted opportunistic screening in these high risk populations.

CONCLUSION

The mortality rate associated with AAA is almost twice as high compared with those without AAA, in a high risk cardiovascular population. Opportunistic screening for AAA in patients attending for a TTE or LLADS has demonstrated prevalence rates of up to 10 times higher than that observed in population based screening in this study. The proportion of those who are candidates for surgical intervention however is small due to patient comorbidities limiting suitability for surgery and little growth in AAA diameter such that many do not reach treatment threshold. Further research into opportunistic screening should be limited to targeted populations more likely to undergo AAA repair, unless proven interventions to modify general mortality in AAA patients are found.

CONFLICT OF INTEREST STATEMENT AND FUNDING

None.

APPENDIX A. SUPPLEMENTARY DATA

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ejvs.2023.02.075

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