Without treatment, atrial fibrillation increases the risk of stroke three- to five-fold and is independently associated with increased mortality, in addition to increased risk of heart failure, cognitive impairment and dementia.¹⁻⁴ Therapy with orally administered anticoagulant agents can reduce the risk of stroke by two-thirds and reduces mortality by one-quarter.³ Two key groups of undertreated patients are at risk of complications: patients with unrecognized (“silent”) atrial fibrillation, and patients with atrial fibrillation that is not managed appropriately. These patients can be considered as having “actionable” atrial fibrillation, since their identification can lead to specific changes in therapy based on their risk profile.

Community screening for atrial fibrillation is feasible, cost-effective, and can result in the start of appropriate anticoagulant therapy.⁵⁻¹⁵ In a systematic review of 30 studies reporting single time-point screening in a variety of settings,
the prevalence of newly diagnosed atrial fibrillation was 1.0\%, increasing to 1.4\% for patients aged 65 years and older.\textsuperscript{14} Screening with a pulse-check in family practice clinics detects more new atrial fibrillation cases than routine care (incidence 1.63%/yr v. 1.04%/yr).\textsuperscript{6,9} The European Society of Cardiology atrial fibrillation guideline suggests that patients aged 65 years and older should undergo opportunistic screening for atrial fibrillation with a pulse-check, followed by electrocardiogram if irregularity is detected.\textsuperscript{4} This is the only current atrial fibrillation guideline to follow the European Society of Cardiology atrial fibrillation guideline suggests that patients aged 65 years and older should undergo opportunistic screening for atrial fibrillation with a pulse-check, followed by electrocardiogram if irregularity is detected.\textsuperscript{4} This is the only current atrial fibrillation guideline to follow this recommendation. Newer technologies could improve the diagnostic accuracy and efficiency of screening,\textsuperscript{7,8,16} but few direct comparisons of screening methods exist.\textsuperscript{17} Our principal research objective was to determine whether newer technologies are more accurate than a pulse-check for the detection and diagnosis of atrial fibrillation in family practice clinics. Our secondary objective was to determine whether changes in management occurred when actionable atrial fibrillation was detected.

**Methods**

**Setting**

We recruited 22 family practice clinics through the Primary Care Networks in Alberta, the University of Toronto Practice-Based Research Network in Ontario, and other sites known to the investigators. Potential sites completed questionnaires to determine prior research experience and availability of personnel to assist with study tasks. Training was performed by telephone and webinar presentations, with or without in-person visits.

**Study design, screening population and ethics approval**

This was a prospective multicentre cohort study. We recruited a convenience series of participants aged 65 years and older who were attending their family practice clinic for routine appointments in 2015 and 2016. Exclusion criteria were patients being unavailable for follow-up; having a cardiac implantable electronic device; inability to have a blood pressure cuff or electrocardiogram electrodes applied; or previous enrollment in the study. Patients with previously known atrial fibrillation were not excluded. Additional details are included as supplemental material (Appendix 1, available at www.cmajopen.ca/content/6/3/E308/suppl/DC1). Participants provided informed consent. The trial was registered with ClinicalTrials.gov (registration no. NCT02262351).

**Atrial fibrillation screening protocol**

Trained staff performed opportunistic screening for each participant using 3 methods: a 30-second radial pulse-check; single-lead electrocardiogram (HeartCheck, CardioComm Solutions Inc.); and by blood pressure device (WatchBP Home A, Microlife AG). A pulse-check was deemed “positive” if any irregularity was found or if the heart rate was 110 beats/min or faster. Single-lead electrocardiograms were uploaded to a secure server, and the rhythm was determined by one of the study cardiologists (FRQ, RS or JH). Uncertain diagnoses were independently assessed by a second cardiologist, and any discrepancies were resolved by the third cardiologist. The blood pressure device takes 3 consecutive readings and reports “AFib” if all 3 readings have an irregular rhythm. Screening staff were blinded to previous diagnoses of atrial fibrillation, and staff who performed the pulse check were blinded to the results of the other 2 tests.

**Diagnosis of atrial fibrillation**

Participants who received a negative result on all 3 screening tests underwent no further testing or follow-up. All other participants (i.e., those who received a positive result on at least 1 test) underwent 12-lead electrocardiogram. If the electrocardiogram did not show atrial fibrillation, 24-hour Holter monitoring was performed. A diagnosis of “confirmed atrial fibrillation” required a 12-lead electrocardiogram showing atrial fibrillation for the entire tracing or a Holter showing more than 30 seconds of continuous atrial fibrillation. The performance of the screening tests was assessed relative to this gold standard. Participants with confirmed atrial fibrillation were deemed to have “actionable atrial fibrillation” if they were not currently taking an anticoagulant. This follows current Canadian Cardiovascular Society guidelines, which suggest anticoagulation therapy for all patients with atrial fibrillation aged 65 years and older.\textsuperscript{18} Patients with atrial fibrillation were considered to have “adequate anticoagulation” if they were taking a non–vitamin K antagonist oral anticoagulant or warfarin with more than 65\% time in the therapeutic range. Patients with atrial fibrillation were identified to their family physician, and treatment decisions were at these family physicians’ discretion.

**Clinical data collection and follow-up**

Baseline demographic and clinical data included risk factors for atrial fibrillation and thromboembolism. Data from patients with confirmed atrial fibrillation included current medications and time in therapeutic range (from their most recent 6 international normalized ratio results) for those taking warfarin. Patients with confirmed atrial fibrillation received follow-up after 90 (± 14) days to document clinical status, medication, heart rate, blood pressure and health care use.

**Statistical analysis**

Only patients with 1 or more positive test result had confirmatory testing, so it is not possible to estimate the overall sensitivity or specificity for atrial fibrillation detection for each test. However, using discordant results between 2 tests, it is possible to test for differences in sensitivity or specificity using the McNemar test of equality of proportions, as outlined by Schatzkin and colleagues.\textsuperscript{19} Sample size calculations can also be performed using this method (Appendix 1).\textsuperscript{19–22} Calculations used a paired-study design (single-lead electrocardiogram and blood pressure device compared separately with pulse-check) with a 2-sided $\alpha$ of 0.025 for multiple compari-
The prespecified primary outcome was the comparison of sensitivity and specificity between screening tests using the McNemar method. The relative false-positive rates for single-lead electrocardiogram and blood pressure device compared with pulse-check were calculated as outlined by Chock and colleagues.23 Prespecified secondary outcomes included heart rate and blood pressure at baseline and at 90 days for patients with actionable atrial fibrillation; and prescription rates at 90 days for anticoagulant agents and rate- or rhythm-control drugs. Continuous variables are presented as mean and standard deviation (SD), or median and interquartile range (IQR), as needed. Categorical variables were compared using a χ² test and continuous variables using a t test. Data at baseline and follow-up were compared using paired t tests for continuous variables and McNemar test for categorical variables. Analyses were performed using SAS version 9.4.

Ethics approval

The following Research Ethics Boards approved the study: Hamilton Integrated Research Ethics Board; University of Alberta; University of Calgary; Women’s College Hospital; Sunnybrook Health Sciences Centre; Queen’s University.

Results

Demographics of the screened population

Figure 1 shows the flow of participants through the study, including attendance rates for confirmatory testing. A total of 2171 participants were enrolled, with a final study population of 2054. The median number of patients enrolled at each site was 47 (IQR 21–151). Seven sites were in municipalities with a population of less than 25 000 people, and the remainder of sites were in larger urban centres. Table 1 summarizes patient characteristics at baseline. There was a high prevalence of hypertension and diabetes among participants, with lower rates of prior stroke, transient ischaemic attack, systemic embolism, myocardial infarction and heart failure.

Screening results

Figure 1 and Table 2 summarize the results of screening, including true-positives, false-positives, and the positive predictive value of each test. One or more test showed a positive result for 168 participants (8.2%). Only 1 participant had a positive pulse-check criterion of a heart rate faster than 110 beats/min; the remainder of the positive pulse-check results were for irregularity. The median time from a positive pulse-check result to 12-lead electrocardiogram was 1 (IQR 0–140) h; the median time to Holter monitor was 27 (IQR 20–39) d. In the primary analysis (Appendix 1), both single-lead electrocardiogram and the blood pressure device had higher specificity than pulse-check for the detection of atrial fibrillation (p < 0.001).

Characteristics of patients with atrial fibrillation detected on screening

A total of 56 patients had confirmed atrial fibrillation, giving an overall prevalence of screen-detected atrial fibrillation of 2.7%. Patients with confirmed atrial fibrillation (Table 1) were older, more often male, had higher body mass index and higher incidence of comorbidities, including heart failure, hypertension, valvular heart disease and previous cardiac surgery. Among patients with atrial fibrillation, 85.7% had a thromboembolism risk score of 3 or greater (points for congestive heart failure, hypertension, age ≥ 75 yr [doubled], diabetes mellitus, stroke [doubled], presence of vascular disease, age 65–74 yr, female sex). Resting heart rate was higher for patients with atrial fibrillation compared with those who did not have atrial fibrillation, and systolic blood pressure was lower. Of the 56 patients with atrial fibrillation, it was a known diagnosis for 44 patients and a new diagnosis for 12 patients (2.1% and 0.6% of the study population, respectively). There was no significant difference in demographics, heart rate or blood pressure between patients with newly diagnosed and known atrial fibrillation (Appendix 1). Forty-two (95.5%) of the patients with known atrial fibrillation, but none of the patients with newly diagnosed atrial fibrillation, were taking anticoagulant agents at baseline. Thus, 14 patients had actionable atrial fibrillation (0.7% of the study population). Twenty-two of the 56 patients with atrial fibrillation were either not taking anticoagulants or had suboptimal warfarin control (1.1% of the study population).

Health care use and clinical data for patients with atrial fibrillation

Follow-up data were obtained for 51 of the 56 patients with confirmed atrial fibrillation, including 13 patients who had actionable atrial fibrillation (Table 3). At 90 days, 48 of the 51 patients (94%) were receiving anticoagulant therapy, mainly through increased prescription of non–vitamin K antagonist oral anticoagulant agents. The proportion of patients with “adequate anticoagulation” increased from 63% at baseline to 82% (p = 0.024), and from 0% to 77% among the 13 patients with actionable atrial fibrillation. Prescription rates for anti-platelet agents and rate- or rhythm-control agents did not differ between baseline and follow-up, nor were there significant differences in heart rate or blood pressure. Clinical events and health care use data are presented in Table 4.

Interpretation

Single-lead electrocardiogram and the blood pressure device we used had superior specificity to pulse-check for the detection of atrial fibrillation, with 72% and 48% fewer false-positive results, respectively. Furthermore, most of the patients for which actionable atrial fibrillation as detected were given a prescription for anticoagulant agents within 90 days, with 8 of the 10 patients starting anticoagulant therapy for the first time being given a non–vitamin K antagonist. This substantially increased the overall quality of anticoagulation from baseline to 90 days.
We directly compared pulse-checks with newer technologies for the detection of atrial fibrillation in unselected older adults in the primary care setting. Previous indirect comparisons, using systematic reviews of earlier studies, have suggested comparable sensitivity for pulse-check, blood pressure devices and single-lead electrocardiogram, with superior specificity for the latter 2 tests, a finding confirmed here. In a small study that involved selected patients, pulse palpation by a nurse had a lower specificity than single-lead electrocardiograms interpreted by a nurse or general practitioner. In another study, the diagnostic accuracy of a blood pressure device was similar to that of electrocardiograms generated by 2 different single-lead devices and interpreted by a cardiologist, but no comparison with a pulse-check was done. A pulse-check is a simple screening test, with reasonable sensitivity that requires few resources. Whether the improved
specificity of single-lead electrocardiograms and blood pressure devices translates into superior cost-effectiveness requires further analysis and will be presented in a separate study.

The prevalence of newly diagnosed atrial fibrillation (0.6%) in our overall study population was fairly low, although this result was similar to that from other community studies that used single time-point screening. In a study by Svennberg and colleagues, 7173 patients aged 75 or 76 years underwent screening with intermittent single-lead electrocardiogram. Previously unknown atrial fibrillation was found in 0.5% of the patients during their first electrocardiogram. Kearley and colleagues identified newly diagnosed atrial fibrillation in 1.2% of 1000 patients aged 75 years and older using 12-lead electrocardiogram.

Limitations
Our study did not exclude patients with previously known atrial fibrillation. Although it may appear unnecessary to “rediagnose” these patients, this approach can be a valuable way of identifying patients who are not receiving appropriate anticoagulation, triggering a review of their therapy. Indeed, we found a high level of baseline anticoagulant use in this population (95.5%), in contrast to other reports where rates of anticoagulant use were typically 50%–65%. Some reports have suggested that anticoagulant use is increasing among patients with atrial fibrillation in the community, partly through increased uptake of non–vitamin K antagonists. We cannot exclude some sampling bias in our study: participating sites may have been more focused on atrial fibrillation management and participating patients may have been more motivated to have an active role in their health care. Screening populations with lower baseline rates of anticoagulant use would reduce the number of patients needed to screen to detect a single case of actionable atrial fibrillation. Identification of patients with actionable atrial fibrillation did lead to a marked increase in anticoagulant use at 90 days.

Table 1: Baseline characteristics of patients, stratified by presence or absence of confirmed atrial fibrillation

| Characteristic | Overall population | Atrial fibrillation confirmed after screening† | p value |
|---------------|--------------------|-----------------------------------------------|---------|
|               | n = 2054           | Yes n = 56                                     | No n = 1998 |
| Age, yr, mean ± SD | 73.7 ± 6.9     | 78.2 ± 7.0                                    | 73.6 ± 6.8    | < 0.001 |
| Male sex      | 958 (46.6)        | 35 (63)                                       | 923 (46.2)    | 0.016  |
| White ethnicity| 1783 (86.8)       | 53 (95)                                       | 1730 (86.6)   | 0.079  |
| Body mass index (kg/m²), mean ± SD | 28.3 ± 5.6     | 29.9 ± 6.5                                    | 28.2 ± 5.5    | 0.029  |
| Comorbidity   |                    |                                               |             |
| Heart failure | 53 (2.6)           | 14 (25)                                       | 39 (2.0)     | < 0.001 |
| Hypertension  | 1214 (59.1)       | 43 (77)                                       | 1171 (58.6)  | 0.006  |
| Diabetes      | 574 (27.9)        | 20 (36)                                       | 554 (27.7)   | 0.19   |
| Previous stroke, transient ischemic attack, or systemic embolism | 149 (7.3) | 8 (14)                                       | 141 (7.1)    | 0.040  |
| Previous myocardial infarction | 149 (7.3) | 7 (13)                                       | 142 (7.1)    | 0.13   |
| Peripheral vascular disease or aortic atheroma | 86 (4.2) | 5 (9)                                       | 81 (4.1)     | 0.073  |
| Valvular heart disease | 42 (2.0) | 8 (14)                                       | 34 (1.7)     | < 0.001 |
| Previous cardiac surgery | 200 (9.7) | 15 (27)                                       | 185 (9.3)    | < 0.001 |
| Current or former smoker | 1036 (50.4) | 35 (63)                                       | 1001 (50.1)  | 0.067  |
| CHA2DS2-VASc score = 1 | 173 (8.4) | 2 (4)                                       | 171 (8.6)    | 0.23   |
| CHA2DS2-VASc score = 2 | 567 (27.6) | 6 (11)                                       | 561 (28.1)   | 0.004  |
| CHA2DS2-VASc score ≥ 3 or higher | 1314 (64.0) | 48 (86)                                       | 1266 (63.4)  | < 0.001 |
| Heart rate (beats/min), mean ± SD | 70.5 ± 11.80 | 67.3 ± 11.43                                 | 70.4 ± 11.78 | < 0.001 |
| Systolic blood pressure, mm Hg, mean ± SD | 137.9 ± 16.87 | 133.2 ± 17.18                                | 138.0 ± 16.84 | 0.035  |
| Diastolic blood pressure, mm Hg, mean ± SD | 76.4 ± 9.77  | 77.9 ± 11.87                                 | 76.3 ± 9.71  | 0.33   |

Note: CHA2DS2-VASc score = points for congestive heart failure, hypertension, age ≥ 75 (doubled), diabetes mellitus, stroke (doubled), presence of vascular disease, age 65–74 yr, sex class of female, SD = standard deviation.

*Unless otherwise indicated.
†Confirmed atrial fibrillation (AF) required a 12-lead ECG showing AF for the entire tracing, or a Holter monitor showing > 30 s of continuous AF. Only patients with 1 or more “positive” screening tests were sent for confirmatory testing.
thus our convenience series could have resulted in selection bias. Because participants who showed a negative result on all 3 tests did not undergo further testing, the true prevalence of atrial fibrillation was not determined, nor could we calculate the true sensitivity or specificity of each test. In addition, owing to a lack of power, we were unable to compare the sensitivity of the tests for the detection of atrial fibrillation. Previous reports have suggested a high sensitivity (> 92%) and specificity (> 89%) for the types of devices we used.16,17 No single screening method detected atrial fibrillation in all 56 patients with confirmed atrial fibrillation: pulse-check, single-lead electrocardiogram and blood pressure device missed 11, 5 and 17 patients, respectively. Screening at a single time point is a practical approach, but will miss many patients with paroxysmal atrial fibrillation, underestimating the true prevalence in the population.

Table 2: Practical characteristics and performance of the 3 screening tests

| Screening test          | Time taken for test, s, mean ± SD | Screening test result no. (%) | True positive (atrial fibrillation confirmed)* | False positive (atrial fibrillation excluded)* | Positive predictive value % (95% CI) | Relative false positive rate compared with pulse-check |
|-------------------------|-----------------------------------|------------------------------|-----------------------------------------------|-----------------------------------------------|-------------------------------------|---------------------------------------------------|
| Pulse-check             | 42.1 ± 22.5                       | 118 (5.7)                    | 1936 (94.3)                                   | 45                                            | 65                                  | 40.9 (31.7–50.1)                                  | –                                                  |
| Single-lead ECG         | 128.2 ± 82.0                      | 78 (3.8)                     | 1976 (96.2)                                   | 51                                            | 18                                  | 73.9 (63.6–84.3)                                  | 0.28                                               |
| Blood pressure          | 194.8 ± 71.5                      | 79 (3.8)                     | 1975 (96.2)                                   | 39                                            | 34                                  | 53.4 (42.0–64.9)                                  | 0.52                                               |

Note: CI = confidence interval, ECG = electrocardiogram, Neg. = negative, Pos. = positive, SD = standard deviation.

*Numbers refer to all patients who underwent each test who attended confirmatory testing (12-lead ECG ± Holter monitor), so are less than the number screening positive in each case.

Table 3: Baseline and 90-day data for patients with screen-detected atrial fibrillation who completed follow-up

| Characteristic                        | All patients with confirmed atrial fibrillation | Patients with actionable atrial fibrillation |
|---------------------------------------|-------------------------------------------------|---------------------------------------------|
|                                       | Baseline n = 51 90 days n = 51 p value*          | Baseline n = 13 90 days n = 13 p value*      |
| Medications, no. (%)                  |                                                  |                                             |
| Antiplatelet agent                    | 11 (22)                                         | 4 (31)                                      | 0.004                                       |
|                                           | 12 (24)                                         | 5 (39)                                      | > 0.99                                      |
| Beta-blocker                          | 27 (53)                                         | 4 (31)                                      | 0.25                                        |
|                                           | 30 (59)                                         | 7 (54)                                      | > 0.99                                      |
| Non-dihydropyridine calcium antagonist | 8 (16)                                          | 0 (0)                                       | NA                                          |
|                                           | 6 (12)                                          | 0 (0)                                       | NA                                          |
| Digoxin                               | 10 (20)                                         | 2 (15)                                      | NA                                          |
|                                           | 9 (18)                                          | 2 (15)                                      | 0.25                                        |
| Class I antiarrhythmic drug           | 0 (0)                                           | 0 (0)                                       | NA                                          |
|                                           | 1 (2)                                           | 0 (0)                                       | NA                                          |
| Class III antiarrhythmic drug         | 0 (0)                                           | 0 (0)                                       | NA                                          |
|                                           | 1 (2)                                           | 0 (0)                                       | NA                                          |
| Any anticoagulant agent               | 38 (75)                                         | 10 (77)                                     | 0.004                                       |
|                                           | 48 (94)                                         |                                             |                                             |
| Warfarin                              | 16 (31)                                         | 10 (77)                                     | 0.004                                       |
|                                           | 18 (35)                                         |                                             |                                             |
| Non–vitamin K antagonist anticoagulant| 22 (43)                                         | 8 (62)                                      | 0.013                                       |
|                                           | 30 (59)                                         |                                             |                                             |
| Heart rate, beats/min, mean ± SD      | 76.6 ± 11.4                                     | 81.4 ± 12.5                                 | 0.003                                       |
|                                           | 73.2 ± 12.0                                     |                                             |                                             |
| Systolic blood pressure, mm Hg, mean ± SD | 133.9 ± 17.6                                  | 135.3 ± 17.2                                | 0.10                                        |
|                                           | 129.9 ± 15.4                                   | 127.2 ± 16.6                                |                                             |
| Diastolic blood pressure, mm Hg, mean ± SD | 79.0 ± 11.7                                    | 79.5 ± 13.1                                  | 0.63                                        |
|                                           | 76.2 ± 11.1                                    | 77.9 ± 12.8                                  |                                             |
| Time in therapeutic range for those on warfarin, %, mean ± SD | 68.8 ± 23.5                                    | NA                                          | 0.07                                        |
|                                           | 68.1 ± 30.0                                    |                                             |                                             |
| Patients with “adequate anticoagulation,”† no. (%) | 32 (63)                                         | 0 (0)                                       | 0.013                                       |
|                                           | 42 (82)                                         |                                             |                                             |

Note: NA = not applicable, SD = standard deviation.

*Statistical comparisons were made using paired t tests for continuous variables and McNemar’s test for categorical variables. With the latter test, when the sum of discordant pairs was 0, this comparison could not be made (NA).

†Adequate anticoagulation” was defined as either taking a non-vitamin K oral anticoagulant agent, or taking warfarin with a time in therapeutic range > 65%.
monitoring will detect more cases of (mainly paroxysmal) atrial fibrillation. In the study by Svännberg and colleagues, repeated intermittent single-lead electrocardiogram monitoring over 2 weeks increased the prevalence of newly detected atrial fibrillation from 0.5% (on initial electrocardiogram) to 3.0%. However, there is some evidence that those with nonparoxysmal atrial fibrillation carry higher thromboembolic risk, even with a similar thromboembolic risk score. Thus, detection of non-paroxysmal atrial fibrillation may identify those who stand to benefit more from appropriate anticoagulation therapy. Finally, screening in our study was performed opportunistically (i.e., only patients attending their family practice clinic were included). This approach follows the European Society of Cardiology recommendations, but would not identify actionable atrial fibrillation among patients who did not attend their clinic. However, in a cluster randomized study, Fitzmaurice and colleagues found no difference in new atrial fibrillation detection between an opportunistic approach and a systematic approach of invitation for screening in detection of atrial fibrillation in patients aged 65 or over: cluster randomised controlled trial. BMJ 2007;335:383-6.

Table 4: Clinical events and health care use for patients with atrial fibrillation detected on screening who completed 90-day follow-up

| Clinical event                              | Confirmed atrial fibrillation, no. (%)* | Actionable atrial fibrillation, no. (%)* |
|---------------------------------------------|----------------------------------------|----------------------------------------|
| Stroke, transient ischemic attack, or systemic embolism | 0 (0)                                  | 0 (0)                                  |
| Myocardial infarction                       | 0 (0)                                  | 0 (0)                                  |
| Heart failure with admission to hospital    | 1 (2)                                  | 0 (0)                                  |
| Major bleed                                 | 0 (0)                                  | 0 (0)                                  |
| Death                                       | 0 (0)                                  | 0 (0)                                  |
| Health care use silence                     |                                        |                                        |
| Emergency department visit                  | 10 (20)                                | 1 (8)                                  |
| No. of emergency department visits          | 14                                     | 1                                      |
| Admission to hospital                       | 4 (8)                                  | 0 (0)                                  |
| No. of admissions                           | 5                                      | 0                                      |
| Family physician visits                     | 36 (71)                                | 10 (77)                                |
| No. of family physician visits              | 84                                     | 26                                     |
| Specialty clinic visits                     | 15 (30)                                | 4 (31)                                 |
| No. of specialty clinic visits              | 17                                     | 5                                      |

Conclusion

Both single-lead electrocardiogram and blood pressure devices showed superior specificity than a manual pulse-check for the detection of atrial fibrillation. Most patients with actionable atrial fibrillation detected on screening started to receive appropriate anticoagulant therapy within 90 days. Multiple studies have now shown that screening for atrial fibrillation in the community can identify patients with undertreated cases. It remains unknown whether screening for atrial fibrillation translates to fewer strokes and other complications.

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Research

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