Organized Blood Pressure Control Programs to Prevent Stroke in Australia
Would They Be Cost-Effective?

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Background and Purpose—High blood pressure (BP) is the most important modifiable stroke risk factor. Worldwide high BP in many people is uncontrolled or people are unaware of their BP status. We aimed to assess whether a program of organized multidisciplinary care and medication would be cost-effective for improving BP control for the prevention of stroke.

Methods—A novel aspect was to simulate the intervention to match recent primary care initiatives (eg, new Medicare reimbursement items) to ensure policy relevance. Current practice and additional costs of each intervention were included using the best available evidence. The differences in the cost per quality-adjusted life year (QALY) gained for the interventions were compared against current practice. Cost-effectiveness was defined as cost per QALY gained was less than Australian dollars (AUD) 50 000 (societal perspective; reference year 2004). The robustness of estimates was assessed with probabilistic multivariable uncertainty analysis.

Results—For primary prevention, the median cost per QALY gained was AUD11 068 (95% uncertainty interval AUD5201 to AUD18 696) in those aged 75 years or older and was AUD17 359 (95% uncertainty interval AUD10 516 to AUD26 036) in those aged 55 to 84 years with ≥15% absolute risk of stroke. Primary prevention interventions were not cost-effective if aged younger than 50 years. The median cost per QALY gained for secondary prevention was AUD1811 and AUD4704, depending on which medications were modeled.

Conclusions—Organized care for BP control targeted at specific populations offers excellent value over current practice. Organized care for secondary prevention provided the greatest benefits and strongest cost-effectiveness. Translation into clinical practice requires improved use of relevant Medicare policy in Australia. (*Stroke*. 2012;43:1370-1375.)

Key Words: economic model ■ primary prevention ■ secondary prevention ■ stroke

Hypertension is the most important modifiable risk factor for stroke. In Australia, ≈42% of cardiovascular disease and ≈7.6% of "all-cause" health loss is attributable to high blood pressure (BP; >140/90 mm Hg).[1] Although effective treatment for high BP exists, the detection and control of high BP remain worldwide problems.[2] In Australia, BP is uncontrolled in ≈8% of people aged older than 25 years and in 60% of treated hypertensive adults.[3] BP may be uncontrolled in treated hypertensive individuals for several reasons, which may include lack of patient compliance with medication or reluctance by physicians to change medications or to prescribe additional medications to achieve BP targets.[4–6] In survivors of stroke, ≈67% at 5 years after a first-ever event receive insufficient treatment to achieve target BP levels.[7] Therefore, improving the control of BP to prevent first-ever

and secondary stroke events should be a public health priority. Currently, no formal national primary care programs to improve the control of BP are used in Australia. The main modifiable risk factors for high BP include diet, especially salt intake, inadequate levels of exercise, obesity, and excessive alcohol intake.[8] Realistic changes in diet and lifestyle have been reported to reduce average BP levels by ≈2 to 3 mm Hg diastolic.[9]

In a recent systematic review, an organized system of regular review and medication (organized care) was found to be the most effective intervention for improving the control of BP.[10] Despite this, there are few data about the value of organized programs that target BP. Moreover, because people often have multiple risk factors, current recommendations are to use an absolute risk approach to cardiovascular disease

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prevention.[11] It is unclear what the impact of applying such programs, whether focused on single risk factor thresholds or based on an individual's combination of risk factors, might be in Australia.

New policy initiatives to improve primary care prevention management could provide the framework to encourage the implementation of organized BP control programs. These policy initiatives provide additional funding to Australian doctors through Medicare reimbursement items and target 3 main groups: those aged 45 to 49 years as part of the Well Person's Health Check; an annual Older Person's Health Assessment for those aged 75 years or older; and for those with existing diseases, such as stroke and diabetes, Chronic Disease Management planning items are available for promoting more individualized and regular multidisciplinary care.[12]

Despite the introduction of these initiatives, there is limited evidence of their effectiveness or cost-effectiveness and there has been inconsistent uptake. Primary care practitioners might be encouraged to use these initiatives and the government might be encouraged to expand the programs if data about the value of such programs were available. We hypothesized that organized care interventions aimed at improving the control and treatment of BP in Australia would be cost-effective compared with current practice management for both the primary and secondary prevention of stroke.

Materials and Methods

Detailed information on the methods and models used in this study is provided in the online-only Supplemental Methods (http://stroke.ahajournals.org). In brief, an established economic microsimulation model was expanded for this project using the updated Model of Resource Utilization Costs and Outcomes of Stroke.[13] The model includes the best available data including stroke incidence and case fatality rates from the North East Melbourne Stroke Incidence Study (NEMESIS)[14] and Australian population statistics by age and gender. The linked spreadsheets enable the reporting of stroke numbers (incident and prevalent cases), lifetime costs, and health outcomes for ischemic stroke and intracerebral hemorrhage.[13] In this present study, new spreadsheets were created to define eligible cases for primary prevention according to each targeted age group (eg, a 45–49 age group was used to conform to eligibility for a Well Person's Health Check). A multidisciplinary reference committee assessed the validity of data inputs and contributed to the interpretation of results, taking into account factors such as equity and feasibility issues, including perceived acceptability to the community.

Costs and benefits were modeled over a lifetime for a 2004 reference year cohort of eligible participants. This reference year was used because it provided the best available data for when the study was undertaken (between 2004 and 2007). Costs and benefits occurring after the first year were discounted using a 3% discount rate to provide net present values. Supplemental Table I (available online at http://stroke.ahajournals.org) provides a summary of the economic evaluation methods used.

Description of Programs Assessed

To make the analysis meaningful, we designed the interventions to conform to the new general practice policy initiatives outlined. When cases were not eligible for a health assessment, a Medicare item for a long consultation was included for the assessment phase (online-only Supplemental Table II). A further novel feature was to include eligibility criteria using an absolute risk threshold for stroke in a separate analysis. That is, the effects of multiple risk factors were taken into account in considering an individual's likelihood of stroke within a 5-year period. Estimation of absolute stroke risk was undertaken using the stroke risk profile Framingham equation applicable to people aged 55 to 84 years (and includes taking into consideration the presence or absence of diabetes, atrial fibrillation, smoking, preexisting coronary heart disease, and cholesterol and BP levels).[15]

Overall, 5 primary prevention pathways were assessed targeting those aged 30 to 69 years (as per the original intervention trial[13] but applied as an effectiveness analysis to Australia), those aged 45 to 49 years; people aged 55 to 84 years with high BP or ≥15% absolute risk of stroke within 5 years, and people aged 75 years or older. Two secondary prevention pathways were also assessed based on achievement of BP goals using different medication regimes (see online-only Supplemental Methods).

Online-only Supplemental Table II provides the care pathway details for each population, including the number of tests and visits. For the secondary prevention models, the 2004 eligible population included all individuals with first-ever strokes and those predicted to be alive in 2004 who had their first-ever stroke between 1987 and 2003 (this is the date range available in the Model of Resource Utilization Costs and Outcomes of Stroke to ensure all eligible prevalent cases are counted in 2004).[13] Cases of transient ischemic attack were also estimated in the ischemic stroke model for this study. The number of incident transient ischemic attack cases was based on a published conservative overall incidence estimate of 0.2%.[16] This estimate was multiplied by the Australian population for 2004 (estimated n=40 224).

The proportion of males and females in each target group of interest (eg, those with or without a history of high BP for certain age bands) and the current practice use of prevention medications were obtained from a large audit of Australian general practices (>16 000 patients; Supplemental Table III available online at http://stroke.ahajournals.org).[17] Two categories of medication use for antihypertensive individuals were established. The current practice mix included the probability of particular medication use regardless of BP level achieved. In contrast, the effective practice mix was the probability of particular medication use when BP was controlled, that is <140/90 mm Hg in treated hypertensive patients. These probabilities were used to establish the cost of medications for the current practice pathway (current practice mix used) and the intervention pathway (effective practice mix used). People at high absolute risk for stroke were assumed to be prescribed aspirin, a cholesterol-lowering agent ("statins") and BP-lowering medication. The effectiveness of the combinations of these drugs used for the absolute risk of stroke treatment scenario was assumed to be multiplicative based on the relative risk reductions expected from each treatment.[18]

Estimating the Number of Strokes Prevented

Because a meta-analysis for BP control interventions demonstrated significant heterogeneity in the pooled estimates,[10] use of these estimates would not have been appropriate for this analysis. Instead, for primary prevention of stroke, we used the study of greatest size and superior quality from this meta-analysis to base the efficacy estimates.[18] In this randomized controlled trial, the intervention group of people aged 30 to 69 years received lifestyle recommendations, in addition to successive titration of antihypertensive medications and free clinical reviews at least every 4 months for up to 5 years.[19] The reported reductions in stroke incidence were consistent across gender, age, and presence of longstanding high BP.[20]

For the secondary (recurrent) stroke prevention effects, we used data from the Perindopril Protection Against Recurrent Stroke (PROGRESS) trial.[21] In this trial, the use of an angiotensin-converting enzyme inhibitor (perindopril) with and without a diuretic (indapamide) was associated with absolute risk reductions over 5 years of 2% for ischemic stroke and 1% for intracerebral hemorrhage.[21] Supplemental Table IV (available online at http://stroke.ahajournals.org) includes a summary of the relative risk reductions for stroke incidence used in this study.

We estimated that 10% of general medical practices in Australia implement the prevention programs. This estimate was based on

evidence in the literature for prevention programs that have no additional Medicare incentive payments (eg, practice nurse payments).[22]

Estimation of Costs

We used a societal perspective to estimate costs. This approach incorporated all direct costs to the health sector, as well as productivity costs (ie, loss of ability to work or engage in leisure activities and household production [unpaid work]), out-of-pocket costs to patients, and the costs of informal care-giving associated with stroke events.[13] Additional time costs for attending clinical visits for the primary prevention interventions were estimated for both employed and unemployed people of working age. For each additional clinic visit, the cost of 1 hour of lost time was attributed to the intervention. Time costs were not included for the secondary prevention interventions because lost time associated with stroke is indirectly captured in the quality of life (quality-adjusted life year [QALY]) measurement.[23]

Cost of medication was based on the 5 most commonly used classes of antihypertensive medications and the probability of prescribing patterns[17] to capture the cost variation and the use of multiple agents per person. The unit prices for medications were obtained from the Pharmaceutical Benefits Schedule.[24] Medicare schedule fees were used as the best estimate of the unit prices for clinician consultations and diagnostic tests.[25]

Supplemental Table V (available online at http://stroke.ahajournals.org) provides a summary of the unit costs for each prevention pathway that was modeled. To cover lag time to effects and management of side effects, different estimates of the costs of treatment were made for the first year and subsequent years of the intervention (Supplemental Tables V and VI, available online at http://stroke.ahajournals.org).

Health Outcomes

Health outcomes were measured as QALYs gained from preventing stroke, with 1 QALY equivalent to 1 year of healthy life.[26] In the present study, we estimated the net difference in the total number of QALYs gained from an intervention over current practice from having prevented first-ever or recurrent strokes. These estimates were calculated for each target group for males and females using quality-of-life data from North East Melbourne Stroke Incidence Study.[26]

Analysis

The design of this study is an incremental cost-effectiveness analysis using population level microsimulation. The net differences in costs and health benefits for each pathway of care against the relevant current practice pathway were estimated as the incremental cost per QALY gained[13] (Figure 1). Interventions in which a cost-saving (negative) result was produced were ranked based on the total health benefits achieved. The interventions that produced more health benefits at an increased cost were considered cost-effective if the cost per QALY gained was less than Australia dollars (AUD) 50 000 per QALY saved. This is a commonly used threshold and is consistent with the decision (or willingness-to-pay) threshold reflected in previous policy decisions for health care programs in Australia.[18] Individual results for males and females and the different stroke types are not presented in this article.

Cost rewards were estimated as the potential cost-offsets obtained from preventing stroke cases attributable to the intervention in 2004. First-ever strokes prevented contributed a lifetime benefit (reward). In contrast, recurrent events only contributed the cost of the first 12 months of treatment. Results without cost-offsets are provided to show the true upfront costs of the interventions because health benefits may not occur in the immediate future.

Sensitivity and Uncertainty Analyses

Univariate (1-way) sensitivity analyses were used to examine the effect of different program options, resulting in larger Medicare payments to increase general practitioner participation. Plausible increases in general practitioner participating were tested from 10%
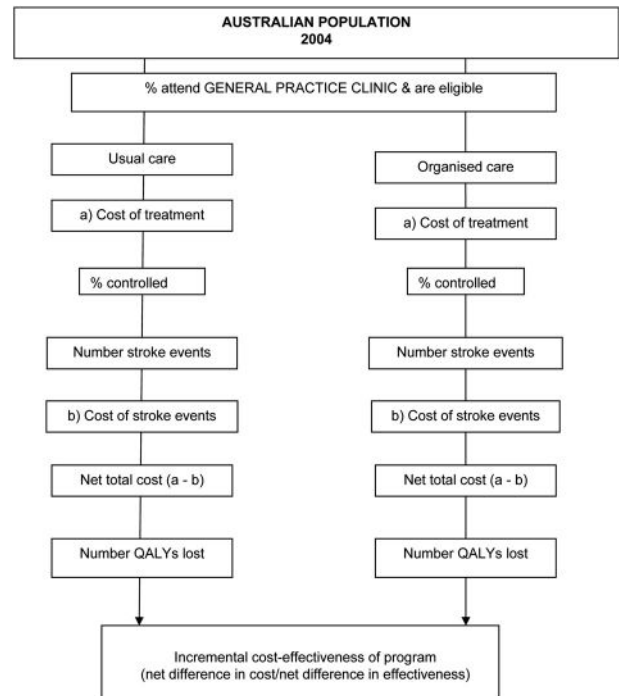
Figure 1. Diagrammatic representation of calculations used to assess cost-effectiveness.

to 26% (for practice nurse payments) and to 70% based on evidence of claims for relevant Medicare practice incentive programs.[27]

Because primary prevention interventions for reducing BP also will have an impact on other cardiovascular disease events, such as heart attack, the costs of preventing stroke are potentially overestimated in this study. Therefore, the costs of the program were apportioned more fairly to stroke as part of uncertainty analyses. We refer to this as joint cost attribution. In this present study, the attribution was based on the reported contribution of stroke to the burden of disease[1] with the program costs varied between 40% and 60%.

Multivariable probabilistic uncertainty analyses of nominated epidemiological and cost variables (online-only Supplemental Table V) were simulated 6000 times using @Risk software version 4.5 (Palisade Corporation). The simulated data were used to estimate a median and 95% uncertainty interval for the outcome measures. Each of the interventions was then ranked in order of cost-effectiveness. In addition, the relative risk reduction for 55- to 84-year-olds, which was based on the overall estimate for 30- to 69-year-olds, was substituted for the 60- to 69-year-old age group's relative risk reduction in an uncertainty analysis, because this may have been more appropriate.

Results

The estimated target populations for 2004 were based on an Australian population of 20.1 million. If 10% of general practitioners adopted the organized care interventions outlined, we then estimated that there would be 117 931 patients with a previous stroke or new transient ischemic attack or stroke in 2004 eligible for the program (Table 1 and online-only Supplemental Table VII). The numbers of eligible patients for the primary prevention interventions ranged from 10 000 to >200 000.

Compared to current practice, interventions of organized management were most cost-effective for those aged 75 years or older (median cost per QALY gained AUD11 764 [95% uncertainty interval, AUD5201 to AUD18 696]), those aged

Table 1. Economic Evaluation Results

Intervention	Eligible Target Group	Intervention Costs* AUD (Million)	Cost Offsets From Strokes Averted AUD (Million)	Net Program Costs† AUD (Million)	Additional Stroke Cases Prevented	QALY Gained	Cost per QALY AUD	Uncertainty Interval Lower Bound (2.5%)	Higher Bound (97.5%)
Secondary prevention									
Any antihypertensive	117 931	82.15	61.40	73.08	1378	6453	1811	Cost saving	8568
ACEi plus diuretic	117 931	106.10	64.48	97.04	2859	6921	4704	Cost saving	10 800
Primary prevention									
Older person's health assessment (age 75 y or older)	43 640	31.19	14.27	27.21	324	1100	11 764	5201	18 696
Absolute risk ≥75% (age 55–84 y)	10 910	7.69	2.11	5.97	40	212	18 201	10 516	26 036
New or uncontrolled BP (age 55–84 y)	140 038	103.10	14.99	91.62	315	1719	44 567	26 033	101 000
Effectiveness analysis (age 30–69 y)	214 831	158.17	7.23	144.76	145	1047	131 366	86 645	267 354
Well Person's Health Check (age 45–49 y)	26 950	20.10	0.46	18.49	9	63	286 253	165 642	598 293

ACEi indicates angiotensin-converting enzyme inhibitor; AUD, Australian dollars; BP, blood pressure; QALY, quality-adjusted life year.

*Total costs of program assuming no one in the eligible target group is already using treatment.

†Net program cost=the total intervention cost for the target group minus the estimated average current practice costs per eligible person who may have already been receiving treatment for high blood pressure in that population group. This represents the true cost of providing the intervention over and above what is currently spent.

55 to 84 years with ≥15% risk of stroke over 5 years (56% male; median cost per QALY gained AUD18 201 [95% uncertainty interval AUD10 516 to AUD26 036]), and those who had already had a stroke event (median cost per QALY gained AUD1811 and AUD4704, depending on the medications used; Table 1). The most cost-effective interventions were those for secondary prevention, which also prevented the greatest number of strokes and remained cost-effective irrespective of whether cost-offsets from the strokes prevented were included or excluded (Figure 2). In uncertainty analyses, between 33% and 65% of the iterations for secondary prevention interventions were cost-saving.

Basing treatment in the 55- to 84-year age group using a BP threshold alone would capture many more eligible cases than when using the absolute risk approach (ie, 140 038 vs 10 910, respectively), but there was only a 60% probability that the former intervention was cost-effective. However, if a proportion of program costs were attributed to the prevention of other vascular diseases, the intervention aimed at people

aged 75 and older would be cost-saving and the program targeting hypertensive 55- to 84-year-olds became cost-effective (median AUD18 692; 95% uncertainty interval, AUD7405 to AUD48 970; Table 2).

When additional Medicare practice incentive payments (eg, these payments are designed to assist with developing infrastructure, such as employment of practice nurses and use of recall registries to improve the quality of care)[28] were assessed in sensitivity analyses, the additional costs associated with these incentives did not alter the ranking of the interventions, but rather increased the potential impact of the programs in preventing stroke (Supplemental Table VIII, available online at http://stroke.ahajournals.org).

Discussion

The results from this study provide new important evidence of the value of an organized system of regular review and medication to improve the control of BP. Our organized care interventions that were developed to be consistent with
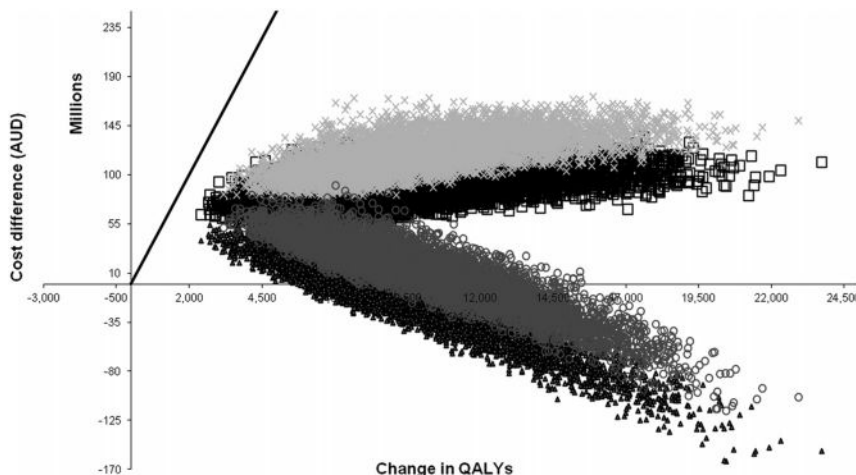
Figure 2. Cost-effectiveness with and without cost-offsets of secondary prevention. The decision threshold was AUD50 000 per quality-adjusted life year (QALY) gained. For the right quadrants, point estimates for the cost per QALY gained that are above the X-axis are cost-effective, whereas those that are below the X-axis are cost-saving. Cost-offsets refer to resources that would be available from the prevention of stroke events. AUD, Australian dollars; −, decision threshold AUD50 000 per QALY saved; □, any medications without cost-offsets; ○, best practice medications with cost-offsets; ▲, any medications with cost-offsets; ×, best practice medications without cost-offsets.

Table 2. Uncertainty Analysis Varying Primary Prevention Intervention Costs as Jointly Attributed Between Heart Disease and Other Vascular Diseases Affected by High Blood Pressure

Cost per QALY Saved*	Mean AUD	Median AUD	95% Uncertainty Interval				% Cost Saving (Total Iterations)
			Lower Bound (2.5%)	Highest Bound (97.5%)	Minimum	Maximum	
Older person's health assessment (age 75 y or older)	Cost saving	Cost saving	Cost saving	4175	Cost saving	10 079	65%
Age 55–84 y							
Absolute risk >15%	3862	3640	Cost saving	9532	Cost saving	15 419	5%
New or uncontrolled BP	21 113	18 692	7405	48 970	2687	88 777	0%
Age 30 to 69 y							
Effectiveness analysis	70 286	64 930	36 938	134 939	23 912	240 118	0%
Well Person's Health Check (age 45–49 y)	148 168	133 649	73 228	307 753	48 420	539 911	0%

Interventions were simulated 6000 times using a range of uncertainty distributions.

AUD indicates Australian dollars; BP, blood pressure; minimum, minimum value obtained from 6000 iterations; QALY, quality-adjusted life year.

*Range for costs attributed to stroke randomly sampled between 40% and 60%.

national primary care initiatives were cost-effective for people aged older than 55 years or who have already experienced a stroke event, regardless of whether additional program elements or practice incentive payments were added. Secondary prevention options provided the largest number of preventable strokes and the greatest potential gain in QALY. This is important because the cumulative risk of recurrent stroke over the course of 10 years is ≈43%, and there remains sizable undertreatment of BP in this population.[7,29]

Currently, no formalized programs focused on improving the control of BP has been adopted in Australia. Data from recent large community surveys provide evidence that many Australians would benefit from having greater awareness of the relationship between BP and stroke, and the issue of uncontrolled BP remains large.[30] Furthermore, there is substantial undertreatment of patients based on the absolute risk assessment of multiple risk factors for cardiovascular disease.[31] We demonstrated the societal value of a broad BP control program for stroke prevention that can address multiple risk factor prevention.

The rationale for investing in treatment starting at age 55 years is also supported by evidence that elevated BP in midlife can increase the risk of stroke when older.[32] Therefore, the potential to treat more people and to prevent a greater number of strokes based on considering BP level alone may be justified. However, the absolute risk approach was more favorable in terms of cost-effectiveness in people aged 55 to 84 years. One could argue that the absolute risk methods derived from the Framingham risk prediction equation are not applicable to Australia. However, several investigators have provided evidence that this equation is reliable for use in Australia.[33–35] A major limitation of the absolute risk approach is that it may underestimate risk in certain populations (eg, Indigenous populations or in those with kidney disease).[33] Therefore, management of risk factors in these circumstances is warranted without full absolute risk assessment. Another relevant point to note was the decision to include aspirin as a primary prevention measure, which subsequently has been found to be of uncertain net value, because the reduction in occlusive events needs to be weighed against any increase in major bleeds.[36] However, removing this element would not have changed the ranking of the interventions. In addition, it was not possible to report on the independent effects of different program elements (such as lifestyle changes and the impact on BP risk factors) using the efficacy summary estimates. Furthermore, changes in population awareness of the causes of stroke and better prevention management and treatment of stroke may be additional factors that influence reductions in mortality. These factors may be sources of overestimation in survival benefits.

Overall, the results of the present study are consistent with those in other published studies on cardiovascular disease prevention.[37–39] Although, comparisons with the results from the present study are problematic because different assumptions, populations, outcomes, and prevention interventions have been assessed; nonetheless, this literature supports, on face value, that the evidence is consistent.

Conclusions

The aging of the population in many countries means that it is imperative to tackle the prevention of stroke events using strategies that are cost-effective and consistent with current policy initiatives to ensure rapid translation. Few investigators have explored the cost-effectiveness of BP control programs in primary care. This present study is the first to incorporate such an approach for stroke in Australia using economic analysis combined with objective feedback from a broad reference group. A novel aspect was to fit the intervention within current primary care policies to ensure greater relevance. Programs to improve the control of BP in people aged 55 years and older and as secondary prevention were worthwhile and should be established in Australia and elsewhere.

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Disclosures

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