

# Living Alone, Patient Sex and Mortality After Acute Myocardial Infarction

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**BACKGROUND:** Psychosocial factors, including social support, affect outcomes of cardiovascular disease, but can be difficult to measure. Whether these factors have different effects on mortality post-acute myocardial infarction (AMI) in men and women is not clear.

**OBJECTIVE:** To examine the association between living alone, a proxy for social support, and mortality post-discharge AMI and to explore whether this association is modified by patient sex.

**DESIGN:** Historical cohort study.

**PARTICIPANTS/SETTING:** All patients discharged with a primary diagnosis of AMI in a major urban center during the 1998–1999 fiscal year.

**MEASUREMENTS:** Patients' sociodemographic and clinical characteristics were obtained by standardized chart review and linked to vital statistics data through December 2001.

**RESULTS:** Of 880 patients, 164 (18.6%) were living alone at admission and they were significantly more likely to be older and female than those living with others. Living alone was independently associated with mortality [adjusted hazard ratio (HR) 1.6, 95% confidence interval (CI) 1.0–2.5], but interacted with patient sex. Men living alone had the highest mortality risk (adjusted HR 2.0, 95% CI 1.1–3.7), followed by women living alone (adjusted HR 1.2, 95% CI 0.7–2.2), men living with others (reference, HR 1.0), and women living with others (adjusted HR 0.9, 95% CI 0.5–1.5).

**CONCLUSIONS:** Living alone, an easily measured psychosocial factor, is associated with significantly increased longer-term mortality for men following AMI. Further prospective studies are needed to confirm the usefulness of living alone as a prognostic factor and to identify the potentially modifiable mechanisms underlying this increased risk.

**KEY WORDS:** social environment; sex factors; cardiovascular disease.

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## INTRODUCTION

The role of psychosocial factors in the development, management, and prognosis of cardiovascular disease (CVD) is an area of increasing interest. Such factors appear to rival more traditional clinical risk factors in the development of acute myocardial infarction (AMI),<sup>1–3</sup> leading some groups to recommend screening for psychosocial factors when assessing patient risk of CVD.<sup>1,4</sup> In addition to independently increasing the risk of developing CVD, psychosocial factors also affect CVD outcomes, including mortality post-AMI.<sup>3–10</sup>

Although many sex differences in the development and course of CVD have been described,<sup>11,12</sup> it is not clear whether the effects of psychosocial factors on CVD risk and outcomes differ between men and women. Generally, studies have not been designed to address this issue or are limited by the low numbers of female participants, particularly with respect to post-AMI mortality.

To better understand the relative importance of psychosocial variables and patient sex to variations in treatment and outcomes in CVD, we undertook an extensive chart review of all AMI patients in a large urban center in western Canada.<sup>13</sup> Living alone, a proxy for social isolation and decreased social support, was chosen as the exposure of interest, as living arrangements appear to affect mortality post-AMI.<sup>6</sup> Our primary objective was to determine whether living alone represents a significant independent risk factor for mortality post-AMI discharge after adjustment for “traditional” clinical and process of care variables. The secondary objective was to determine whether any observed association between living alone and longer term mortality varied by patient sex.

## METHODS

### Study Participants

Patients from all three adult care hospitals in Calgary, Alberta, discharged between April 1, 1998, and March 31, 1999, with a recorded primary discharge diagnosis of AMI (excluding post-

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MI readmission cases) were identified for possible inclusion in this study from hospital administrative records (*International Classification of Diseases*, ninth revision, code 410).<sup>14</sup> All three facilities are teaching hospitals staffed by a common pool of cardiologists, who operate as a citywide division. Careful review of all available hospital charts ensured that AMI was the final diagnosis in either the discharge summary or the clinical notes. Previous work supports the use of discharge codes as a valid method for identifying AMI patients.<sup>15</sup>

To capture the full process of care for the index AMI event (from hospital admission to discharge), we excluded patients who received part of their care at a hospital outside of Calgary and were subsequently transferred into the city. Other exclusion criteria were the development of AMI in hospital after admission for another medical problem, a discharge diagnosis of query AMI, and residence outside the Calgary health region. Patients who died during their index AMI admission ( $n=78$ ) were also excluded from the analyses given the focus on postdischarge survival. Data from subsequent hospitalizations following an AMI were not collected because of our primary interest in the acute treatment of the captured AMI event.

## Data Collection

A nurse skilled in data abstraction and coding from medical charts for cardiovascular conditions derived data from a thorough review of the available hospital inpatient records. Information regarding patients' sociodemographic, clinical,

and process-of-care characteristics was abstracted and recorded on a standardized form. Sociodemographic and clinical items included age, sex, marital status, key contact/next of kin, current living arrangement, residence (postal code), time of symptom onset, time and date of arrival at the emergency department, time and date of in-hospital death (if applicable), history of comorbid conditions and allergies, and lifestyle behaviors (smoking, drinking). Living alone was determined by a combination of marital status (single, divorced, or widowed), absence of a key contact with the same address, phone number or postal code, and any notes about the patient's living arrangements. Lodge, assisted-living, and long-term-care-facility residents were categorized as living with others. A history of various comorbid conditions was recorded as present if documented in the medical chart for the captured admission; otherwise, the condition was recorded as absent. Processes of care included cardiac procedures during stay and medication use (by class) during hospitalization (including time to treatment for acetylsalicylic acid and thrombolytic agents) and at discharge. Outcomes were determined by linkage to hospital administrative data, as well as vital statistics. This study received ethical approval from the Health Research Ethics Board of the University of Calgary.

## Statistical Analyses

Patient sociodemographic characteristics, comorbid conditions, clinical factors, and process-of-care factors were compared

**Table 1. Baseline Sociodemographic, Clinical, and Process-of-Care Characteristics of Patients Admitted for Acute Myocardial Infarction According to their Living Arrangements Prior to Hospital Admission, Fiscal Year 1998–1999 ( $n=880$ )**

Characteristic	Total sample $n=880$	Living alone $n=164$	Living with others $n=716$
Age (mean years $\pm$ SD)*	65.4 $\pm$ 13.5	70.1 $\pm$ 13.9	64.3 $\pm$ 13.2
$\geq 75$ years*	231 (26.3%)	71 (43.3%)	160 (22.4%)
Women*	276 (31.4%)	86 (52.4%)	190 (26.5%)
Current smoker	330 (37.5%)	70 (42.7%)	260 (36.3%)
Hypertension	416 (47.3%)	76 (46.3%)	340 (47.5%)
Hypercholesterolemia <sup>†</sup>	324 (36.8%)	43 (26.2%)	281 (39.3%)
Diabetes	150 (17.1%)	26 (15.9%)	124 (17.3%)
Previous myocardial infarction	235 (26.7%)	47 (28.7%)	188 (26.3%)
Cerebrovascular disease <sup>‡</sup>	73 (8.3%)	19 (11.6%)	54 (7.5%)
Chronic obstructive pulmonary disease	98 (11.1%)	21 (12.8%)	77 (10.8%)
Congestive heart failure <sup>†</sup>	42 (4.8%)	15 (9.2%)	27 (3.8%)
Peripheral vascular disease	73 (8.3%)	15 (9.2%)	58 (8.1%)
Alcohol abuse	83 (9.4%)	14 (8.5%)	69 (9.6%)
Presentation within 1 hour <sup>§//</sup>	184 (20.9%)	24 (14.6%)	160 (22.4%)
Left ventricular ejection fraction <sup>//</sup>			
Not measured	377 (42.8%)	80 (48.8%)	297 (41.5%)
<30%	31 (3.5%)	10 (6.1%)	21 (2.9%)
30%–50%	185 (21.0%)	29 (17.7%)	156 (21.8%)
>50%	287 (32.6%)	45 (27.4%)	242 (33.8%)
Median length of stay <sup>†</sup>	7.0 $\pm$ 10.1	9.0 $\pm$ 9.9	7.0 $\pm$ 10.2
Catheterization <sup>‡</sup>	621 (70.6%)	106 (64.6%)	515 (71.9%)
Thrombolysis	205 (23.3%)	37 (22.6%)	168 (23.5%)
Acetylsalicylic acid (in hospital)	843 (95.8%)	154 (93.9%)	689 (96.2%)
Beta-blocker (in hospital)	713 (81.0%)	129 (78.7%)	584 (81.6%)
Post MI congestive heart failure (in-hospital complication)	130 (14.8%)	27 (16.5%)	103 (14.4%)

MI=myocardial infarction

\*Difference between comparison groups is statistically significant:  $P \leq .0001$

<sup>†</sup>Difference between comparison groups is statistically significant:  $P < .01$

<sup>‡</sup>Difference between comparison groups is statistically significant:  $P < .10$

<sup>§</sup>Patients with no information on time to presentation from symptom onset ( $n=160$ ) were assumed to have a time to presentation of greater than 1 hour

// Difference between comparison groups is statistically significant:  $P < .05$

between AMI patients who were living alone and those living with others at the time of hospitalization. Bivariate associations were examined using cross-tabulations and  $\chi^2$  tests of significance for categorical variables and *t* tests for continuous variables. The Mann-Whitney-Wilcoxon test was used to compare median times for length of stay. Bivariate associations between the sociodemographic, clinical, and process-of-care variables and mortality were examined using univariate Cox proportional hazards regression models. The outcome of interest was survival among those who survived their index stay, with time measured from date of discharge to either date of death, as captured in vital statistics data, or to the end of follow-up on December 31, 2001. Multivariate Cox proportional hazards regression models were used to examine the independent effect of living alone on patient survival following adjustment for potential clinical and process-of-care confounding factors using backward elimination. Adjusted survival curves were generated from Cox proportional hazards models using the corrected group prognosis method.<sup>16,17</sup> All statistical analyses were performed using SAS for Windows (release 9.1).

## RESULTS

Of 880 patients, 164 (18.6%) were living alone at the time of hospital admission for AMI (Table 1). These patients were

significantly different from their counterparts. On average, patients living alone were twice as likely to be aged greater than 75 years and to be female. The two groups were similar in terms of lifestyle practices (smoking and alcohol use), medication use, and baseline clinical conditions, with a few exceptions. Relative to patients living with others, those living alone were significantly more likely to have cerebrovascular disease, congestive heart failure (CHF), and poor left ventricular ejection fraction (LVEF), but were less likely to have hypercholesterolemia. Patients living with others were significantly more likely to present within an hour of the onset of symptoms and to have cardiac catheterization following admission for AMI, although there was no difference between the two groups in the use of thrombolysis. There was also a significant difference in the median length of stay for patients living alone (9 days) versus those living with others (7 days).

The unadjusted and adjusted hazards ratios (HR) for mortality extending over 3 years postdischarge for the index AMI are presented in Table 2. The sample size for these analyses was 802 (excluding 78 patients who died during hospitalization). Living alone was significantly associated with poorer survival postdischarge at the bivariate level [HR 2.2, 95% confidence interval (CI) 1.4-3.3]. Female sex showed a trend towards increased mortality. In the unadjusted analyses, both women and men living alone showed a significantly increased risk of mortality postdischarge. Furthermore, in-

**Table 2. Estimated Unadjusted and Adjusted Hazards Ratios †(95% CI) for Mortality Extending over 3 Years Post-Discharge by AMI Patients' Baseline Sociodemographic, Clinical and Process of Care Characteristics, Fiscal Year 1998/99 (n=802 ‡)**

Characteristic	Unadjusted HR (95% CI)	Adjusted HR (95% CI)
Living alone	2.16 (1.42-3.31)	-
Women	1.40 (0.94-2.11)	-
Living arrangement - Sex		
Men living alone	2.28 (1.28-4.07)	2.01 (1.10-3.68)
Women living alone	2.38 (1.35-4.18)	1.21 (0.66-2.19)
Women living with others	1.31 (0.78-2.18)	0.86 (0.51-1.46)
Men living with others (reference)	1.00	1.00
≥75 years	5.59 (3.77-8.30)	3.13 (1.97-4.97)
Current smoker	2.05 (1.31-3.23)	-
Hypertension	1.11 (0.75-1.64)	-
Hypercholesterolemia	1.09 (1.04-1.15)	-
Diabetes	1.18 (0.72-1.95)	-
Previous myocardial infarction	1.47 (0.97-2.23)	-
Cerebrovascular disease	3.17 (1.90-5.27)	-
Chronic obstructive pulmonary disease	2.05 (1.23-3.41)	-
Congestive heart failure	5.49 (3.12-9.66)	2.40 (1.29-4.47)
Peripheral vascular disease	3.17 (1.94-5.17)	2.02 (1.22-3.37)
Alcohol abuse	1.28 (0.62-2.64)	-
Presentation within 1 hour <sup>†</sup>	0.50 (0.28-0.92)	-
Left ventricular ejection fraction		
Not measured	7.27 (3.62-14.58)	3.46 (1.66-7.24)
<30%	7.98 (2.84-22.41)	2.85 (0.93-8.72)
30%-50%	3.17 (1.43-7.07)	2.49 (1.11-5.58)
>50% (reference gp)	1.00	1.00
Catheterization	0.24 (0.16-0.36)	0.56 (0.36-0.88)
Thrombolysis	0.51 (0.29-0.89)	-
Acetylsalicylic acid (in hospital)	0.29 (0.13-0.65)	-
Beta-blocker (in hospital)	0.36 (0.23-0.54)	-
Post-MI congestive heart failure (in-hospital complication)	2.90 (1.88-4.47)	2.19 (1.38-3.48)

HR=hazard ratio, CI=confidence interval, MI=myocardial infarction † Obtained from multivariate Cox proportional hazards models, adjusted for variables listed in column, includes only those variables retained after backward elimination of non-significant variables

‡ Sample size excludes 78 patients who died during their index AMI hospital stay.

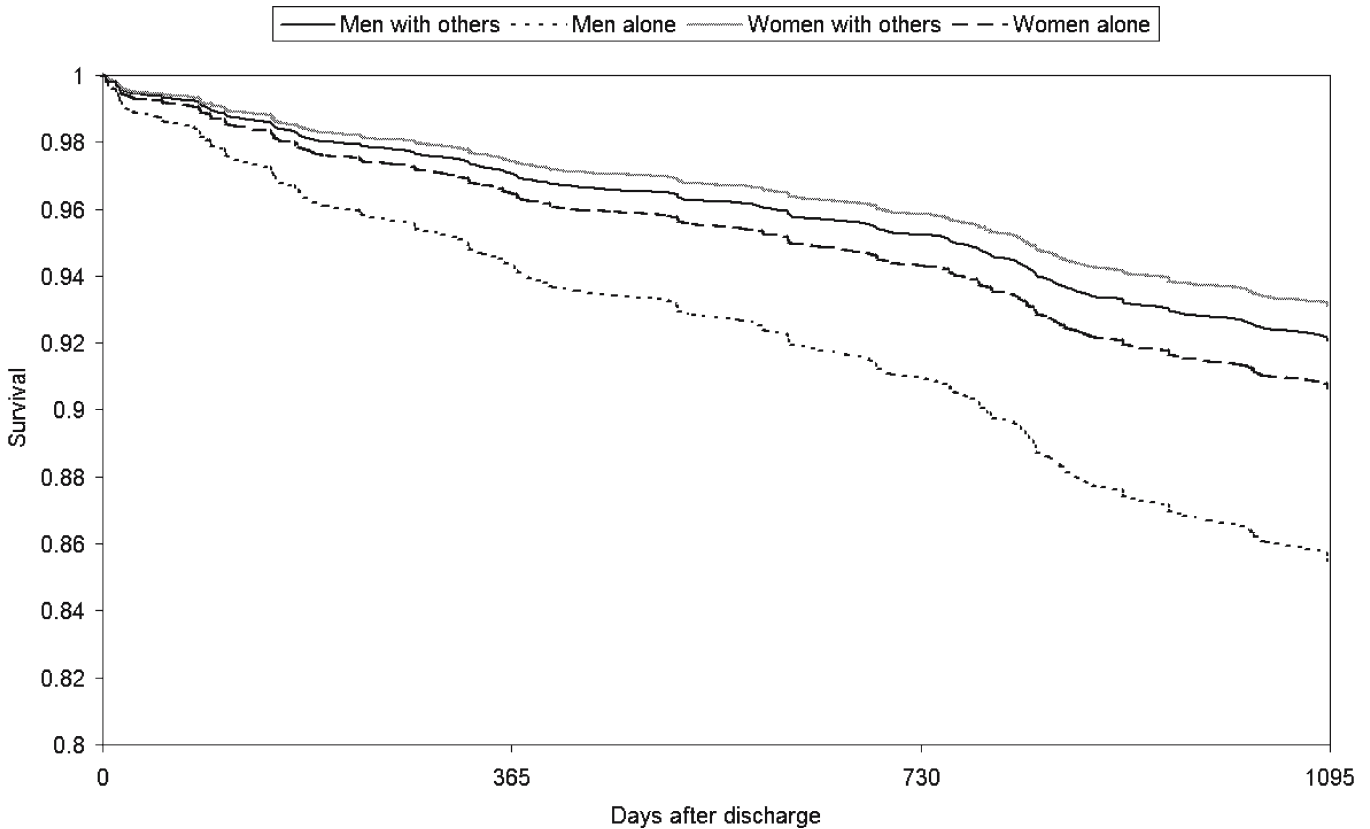


Figure 1. Adjusted (for age  $\geq 75$  years, comorbidities (congestive heart failure, peripheral vascular disease), left ventricle ejection fraction, catheterization, post-myocardial infarction congestive heart failure) survival curves over 3 years postdischarge (sample size excludes 78 patients who died during their index acute myocardial infarction (AMI) hospital stay) for AMI stratified by living arrangement and patient sex.

creased patient age ( $\geq 75$  years); current smoking; and the presence of hypercholesterolemia, cerebrovascular disease, chronic obstructive pulmonary disease, CHF (both at admission and as a post-AMI complication during stay), peripheral vascular disease, and poor LVEF were significantly associated with postdischarge mortality. The receipt of an angiotensin-converting enzyme inhibitor during hospitalization was also associated with a significantly higher risk of postdischarge mortality; however, because of collinearity concerns with other covariates (e.g., CHF), this variable was not retained in our analyses. Conversely, patient presentation within 1 hour of symptom onset and the receipt of cardiac catheterization, thrombolysis, acetylsalicylic acid, and a beta-blocker during hospitalization were associated with a significantly lower risk of mortality post-AMI.

Following adjustment for all clinical and process-of-care variables, living alone was significantly associated with increased mortality (adjusted HR 1.6, 95% CI 1.0–2.5; data not shown). With stratification of living alone status by patient sex, living alone significantly increased the risk of death postdischarge in men (adjusted HR 2.0, 95% CI 1.1–3.7) but not in women (adjusted HR 1.2, 95% CI 0.7–2.2). There was a trend towards a gradient of decreasing mortality, with men living alone having the highest risk, followed by women living alone, men living with others, and women living with others. Further analyses adjusting for all clinical, health, and process-of-care variables significant at the bivariate level did not significantly

alter these findings. The corresponding risk-adjusted survival curves for these four groups are presented in Figure 1.

## DISCUSSION

In this community-based historical cohort study, living alone was an independent risk factor for mortality following hospital discharge for AMI. However, the observed association between living alone and postdischarge mortality also varied by patient sex. While AMI patients living alone were significantly more likely to be older women, the increased mortality risk associated with living alone remained significant for men, but not for women, after adjustment for potentially confounding clinical and process-of-care variables.

Several investigations have shown an independent relationship between social support or social networks and patient outcomes following AMI.<sup>3,5–10</sup> However, there is no consensus on the definition or best measure of these psychosocial factors. Living alone is an objective, easily defined exposure, associated with adverse health outcomes in a wide variety of patient populations, including older adults and young HIV-infected patients.<sup>18–22</sup>

Our finding that patients' living arrangements may pose a more significant AMI mortality risk for men as compared with women is consistent with other patient populations. Living alone was shown to be a significant risk factor for CVD

morbidity and mortality among hypertensive men, but not women.<sup>18</sup> Men living alone were at greater risk than women living alone for respiratory disease–related death<sup>19</sup> and all-cause mortality<sup>20</sup> in other study populations. However, there appear to be few investigations of the potential interaction between patient sex and living arrangements in relation to risk for AMI outcomes in particular.<sup>5,6,23</sup>

In the Multicenter Diltiazem PostInfarction Trial, living alone was a significant independent risk factor for a combined outcome of recurrent nonfatal infarction or cardiac death up to 4 years post-AMI.<sup>6</sup> There was also a nonsignificant elevated risk of recurrent cardiac events post-AMI in women compared with men living alone in this study.<sup>6</sup> While adverse outcomes post-AMI, including 1-year mortality, were more likely in patients living alone in the Global Use of Strategies To Open occluded coronary arteries (GUSTO)-III trial, these differences did not persist after adjustment.<sup>23</sup> Furthermore, patient sex did not significantly interact with living alone in any of the models in GUSTO-III.<sup>23</sup> Living alone, depressive symptoms, marital status, and living arrangements were not associated with 6-month mortality post-AMI in the New Haven Established Populations for the Epidemiologic Study of the Elderly AMI program.<sup>5</sup> Low emotional social support, the only significant psychosocial risk factor for mortality in this study, affected men and women similarly post-AMI.<sup>5</sup>

Methodological differences may explain, in part, the apparent inconsistent findings regarding the relevance of patient sex to the observed association between living alone and adverse outcomes post-AMI. For example, the New Haven longitudinal community-based cohort study was restricted to AMI patients aged 65 years and older who were hospitalized for AMI during the 1980s.<sup>5</sup> Further, the more recent studies involved randomized controlled trial data, thus potentially limiting their findings to a more select sample of younger and healthier patients.<sup>6,23</sup>

Psychosocial factors may affect the course or development of CVD through one or more of the following: psychological, biological, behavioral, or process-of-care pathways. Various theories have been proposed and reviewed elsewhere<sup>2,3,10</sup>; yet, it is unclear how these mechanisms might be affected by patient sex. Our findings may suggest a differential vulnerability of men to living alone through one or more of these pathways.

AMI patients are vulnerable to psychological stress, depression, and anxiety, all of which have been associated with adverse cardiovascular outcomes.<sup>3,7,9,10</sup> Previous work suggests there are sex differences in reporting depressive symptoms post-AMI (women more likely to report)<sup>7,9</sup> and in the association between living alone and depression post-AMI (men living alone more likely depressed).<sup>7</sup> Despite these differences, depression did not appear to account for differences in MI recurrence between men and women post-AMI.<sup>7</sup> Although we could not explore the relevance of depression as a potential confounding or effect-modifying factor in our analyses, previous findings and the diverse range of plausible underlying mechanisms argue against depression acting as the sole mediator of the association between living alone and mortality post-AMI.

Sex-specific biological responses to living alone represent another possible mechanism underlying the poorer survival post-AMI observed for men. As with other stressful stimuli, living alone may lead to alterations in neurohormonal systems

(e.g., the hypothalamic–pituitary–adrenal axis and the sympathetic system), as well as proinflammatory and hypercoagulable states.<sup>2,3,10,24,25</sup> Neurohormonal and inflammatory factors have been associated with “traditional cardiovascular risk factors” (including hypertension and insulin resistance) and, independently, with the development of atherosclerotic disease and poorer outcomes in CVD.<sup>2,3,10,24,25</sup> Male and female animals exposed to stress appear to develop atherosclerotic disease via different biological pathways.<sup>24</sup> In humans, different types of stresses provoke stronger biological responses in women as opposed to men.<sup>25</sup> However, the exact nature of the biological response to living alone, and whether it differs in men and women, does not appear to have been studied.

Psychosocial factors, including living alone, may also affect survival post-AMI differently in men and women by altering health-related behaviors.<sup>2,3,10</sup> Social isolation tends to be associated with higher risk behaviors.<sup>2,3</sup> Notably, in the current study, patients living alone did not differ from those living with others in terms of smoking or alcohol abuse. Living alone may also be associated with poorer adherence with medication and other treatment and/or follow-up recommendations, and this association may vary by patient sex. Unfortunately, data on these behaviors posthospitalization were not available in our study. Interestingly, men appear to be more reliant on the encouragement of their spouses to seek medical attention for cardiovascular symptoms, in contrast with women, who rely more on other relatives.<sup>26</sup> However, the difference in mortality for men living alone in this study was independent from delayed presentation after symptom onset.

Living alone may also affect coping strategies differently in men and women post-AMI. Men appear to turn to their spouses preferentially for support, rather than to other family members, perhaps making them more vulnerable to living alone.<sup>8,26</sup> Returning to household chores and activities is an important coping strategy for some women post-AMI, potentially placing women living with others at higher risk by increasing their activity level more quickly than women living alone.<sup>26</sup> Women may also increase their workload to make lifestyle changes post-AMI without affecting other members of their household (e.g., cooking one meal for the family and one meal for themselves).<sup>26</sup> Women may also avoid cardiac rehabilitation because of family obligations.<sup>27</sup> Although data regarding patients' coping strategies and lifestyle changes were not available in the present study, we did not observe an increased vulnerability post-AMI for women living with others.

While it is important to identify psychosocial factors affecting outcomes in AMI and the mechanisms involved, the ultimate goal is to identify interventions that are able to mitigate these effects. Further study is required to determine whether interventions designed to compensate for the risk posed by men living alone are effective at reducing mortality post-AMI. Unfortunately, the recent trials involving the pharmacological and nonpharmacological management of depression post-AMI<sup>3,28</sup> illustrate the potential barriers involved in such research. For example, despite the strong association between depression (a treatable medical condition) and adverse outcomes post-AMI, it has been difficult to show that successfully treating depression reduces the associated increased risk.<sup>28</sup> While it will likely be more difficult to study interventions targeting psychosocial factors in AMI, it is no less important than addressing conventional biomedical aspects of CVD given the significant contribution of these factors to



patient outcomes. Furthermore, to be effective, these interventions will need to consider potential sex differences in the pathways leading to adverse outcomes for socially vulnerable patient groups. In the absence of evidence regarding appropriate interventions, an important first step will be for clinicians to include patients' living arrangements as one of many prognostic factors in need of care planning to optimize outcomes post-AMI.

## Strengths and Limitations

The current study has several strengths, including a complete year-long census of all AMI patients in a large urban center, with no age restriction and limited exclusion criteria. Patients were followed for up to 3 years postdischarge from hospital and outcomes were determined via linkage to vital statistics. The data were collected more recently than previous studies examining living alone in AMI.<sup>5,6,23</sup> Detailed data collection allowed concomitant analysis of psychosocial, clinical, and process-of-care factors, and the comprehensiveness of the chart review allowed for the incorporation of potentially relevant confounding factors in our survival models. While the use of data from a single urban center could potentially limit generalizability, the finding that living alone and patient sex adversely affect AMI mortality in an urban Canadian center with relatively high resources, high levels of access to care, and low cardiovascular mortality suggests a meaningful clinical concern.<sup>29</sup>

Although retrospective in study design, the systematic chart review form was carefully designed and tested by key investigators prior to data collection. The use of living alone as the exposure of interest is advantageous in that it provides an objective, concrete, psychosocial variable that can be determined without special scales or measures, unlike social support or social network variables. The determination of living arrangements was calculated indirectly, but incorporated information from multiple sources within the hospital chart. The consistency regarding the basic demographic characteristics of patients living alone (described in Table 1) with expected values and previous studies<sup>6,23</sup> also supports the validity of this measure. Finally, the absence of information regarding patients' socioeconomic status and mental health (particularly depression) limited our ability to explore potential causal pathways and mediating factors.

## CONCLUSION

We found that living alone, an easily measured psychosocial factor, was associated with increased mortality post-AMI discharge but that the association was modified by patient sex. While AMI patients living alone were more likely to be older women, the effect on mortality was significant for men living alone. Further prospective studies are required to confirm the usefulness of living alone as a prognostic factor in clinical practice, and to help identify the potentially modifiable mechanisms underlying this association.

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**Potential Financial Conflicts of Interest:** None disclosed.

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