Comparison of Mortality Between Private For-Profit and Private Not-For-Profit Hemodialysis Centers
A Systematic Review and Meta-analysis

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MORE THAN 20 YEARS AGO, Relman and Rennie[1] suggested that profit status may affect dialysis practices. Advocates of private for-profit health care delivery argue that for-profit providers can deliver high-quality care more efficiently than not-for-profit providers.[2] However, fears that for-profit facilities compromise quality of care to maintain shareholder returns[3,4] have precipitated a heated debate about whether the profit status of hemodialysis facilities influences patient mortality.[5-7]

Separating issues of funding (ie, who will pay for the health care) and delivery (ie, who owns and administers the institutions providing care) helps to in-

Context Private for-profit and private not-for-profit dialysis facilities provide the majority of hemodialysis care in the United States. There has been extensive debate about whether the profit status of these facilities influences patient mortality.

Objective To determine whether a difference in adjusted mortality rates exists between hemodialysis patients receiving care in private for-profit vs private not-for-profit dialysis centers.

Data Sources We searched 11 bibliographic databases, reviewed our own files, and contacted experts in June 2001–January 2002. In June 2002, we also searched PubMed using the "related articles" feature, SciSearch, and the reference lists of all studies that fulfilled our eligibility criteria.

Study Selection We included published and unpublished observational studies that directly compared the mortality rates of hemodialysis patients in private for-profit and private not-for-profit dialysis centers and provided adjusted mortality rates. We masked the study results prior to determining study eligibility, and teams of 2 reviewers independently evaluated the eligibility of all studies. Eight observational studies that included more than 500 000 patient-years of data fulfilled our eligibility criteria.

Data Extraction Teams of 2 reviewers independently abstracted data on study characteristics, sampling method, data sources, and factors controlled for in the analyses. Reviewers resolved disagreements by consensus.

Data Synthesis The studies reported data from January 1, 1973, through December 31, 1997, and included a median of 1342 facilities per study. Six of the 8 studies showed a statistically significant increase in adjusted mortality in for-profit facilities, 1 showed a nonsignificant trend toward increased mortality in for-profit facilities, and 1 showed a nonsignificant trend toward decreased mortality in for-profit facilities. The pooled estimate, using a random-effects model, demonstrated that private for-profit dialysis centers were associated with an increased risk of death (relative risk, 1.08; 95% confidence interval, 1.04-1.13; $P<.001$). This relative risk suggests that there are annually 2500 (with a plausible range of 1200-4000) excessive premature deaths in US for-profit dialysis centers.

Conclusions Hemodialysis care in private not-for-profit centers is associated with a lower risk of mortality compared with care in private for-profit centers.
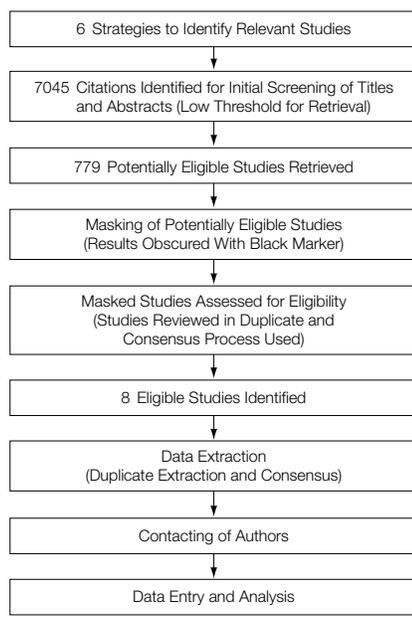
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Figure 1. Flowchart of Methodological Steps in the Systematic Review

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│ 6 Strategies to Identify Relevant Studies │
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│ 7045 Citations Identified for Initial Screening of Titles │
│ and Abstracts (Low Threshold for Retrieval) │
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│ 779 Potentially Eligible Studies Retrieved │
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│ Masked Studies Assessed for Eligibility │
│ (Studies Reviewed in Duplicate and │
│ Consensus Process Used) │
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│ 8 Eligible Studies Identified │
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│ Data Extraction │
│ (Duplicate Extraction and Consensus) │
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│ Contacting of Authors │
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│ Data Entry and Analysis │
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form debates about health care systems. Both funding and delivery can occur through private or public means. Private funding or delivery can be for profit or not for profit. Private for-profit and private not-for-profit insurance companies use insurance premiums to pay for the health care of the patients they insure. Delivery of care can occur at private for-profit institutions that are owned by investors or at private not-for-profit institutions that are owned by communities, religious organizations, or philanthropic groups. Public funding indicates payment by the government, and public delivery indicates that a health care institution is owned and administered by the government. All public health care institutions are not for profit.

Since 1973, the US government has, through Medicare, funded the care of patients receiving dialysis.[8] Currently in the United States, private for-profit (approximately 75%) and private not-for-profit (approximately 20%) facilities provide most hemodialysis care.[9] Public institutions deliver the small remaining proportion of hemodialysis care.

Our study addresses issues of health care delivery, rather than health care

funding. Accurate understanding of the impact of alternative health care delivery systems requires a systematic, comprehensive, and unbiased accumulation and summary of the available evidence. We therefore undertook a systematic review and meta-analysis to address the following question: what is the relative impact of private for-profit vs private not-for-profit delivery of hemodialysis care on patient mortality?

METHODS

This systematic review is part of a series of reviews we are undertaking comparing health outcomes, appropriateness and quality of care, and costs in private for-profit and private not-for-profit health care institutions. We have previously reported on hospital mortality rates in private for-profit and private not-for-profit hospitals.[10] **FIGURE 1** outlines the methodological steps for this systematic review. The Hamilton Health Sciences Research Ethics Board in Hamilton, Ontario, approved this study protocol.

Data Sources

We undertook 6 strategies to identify potentially eligible studies. Our search included 11 electronic bibliographic databases, our own files, and contact with experts. We further searched PubMed using the "related articles" feature, SciSearch, and the reference lists of all studies that fulfilled our eligibility criteria.

A medical librarian used all the studies of which we were initially aware to identify Medical Subject Heading terms and key words for the search. In each database, the librarian undertook an iterative process to refine the search strategy through testing of several search terms and incorporation of new search terms as new relevant citations were identified. The search included the following databases: EMBASE (1980-2001), MEDLINE (1966-2001), Health-STAR (1975-2001), CINAHL (1982-2001), BIOETHICSLINE (1973-2000), Wilson Business Abstracts (1997-2001), EconLit (1969-2001), Cochrane Library (2001, issue 3), Dis-

sertation Abstracts Ondisc (1861-2001), ABI (Abstracted Business Information)/Inform (1970-2001), and NTIS (National Technical Information Service) (1964-2002). Complete descriptions of the database search strategies are available from the authors.

Study Selection

Eligibility Criteria. We included published and unpublished observational studies and randomized controlled trials that directly compared the mortality rates of hemodialysis patients in private for-profit and private not-for-profit dialysis centers. Eligible observational studies had to provide adjusted mortality rates or mortality rates from matched cases.

Screening Process. Our 6 search strategies identified 7045 unique citations. Teams consisting of 2 individuals independently screened the titles and abstracts of each citation and identified all citations for full review where there was any possibility that the study contained a comparison in which we were interested. This screening process yielded 779 full-text publications identified by one or both screeners for full review (Figure 1).

Assessment of Study Eligibility. We masked the results (ie, we obscured them from the tables and text using a black marker) of all publications selected for full review. To determine eligibility, teams of 2 reviewers independently evaluated masked articles that they had not assessed during the screening process. When disagreements occurred, the reviewers discussed the reasoning for their decisions, and if one reviewer realized she or he had made an error then the process was complete. This occurred in all cases of disagreement, and, therefore, plans for an independent review of cases of substantive disagreement proved unnecessary. Our agreement on study eligibility was excellent ($\kappa = 0.91$; 95% confidence interval [CI], 0.85-0.97).

Data Extraction

Teams of 2 reviewers independently abstracted the following data from all

studies meeting eligibility criteria: sampling method, source of data (eg, administrative database, patient chart), type of dialysis facilities evaluated (ie, freestanding, hospital-based, or both), dates when data collection was initiated and completed, duration of patient follow-up, number of private for-profit and private not-for-profit dialysis facilities and patients evaluated, mortality, potential confounders adjusted for in the analyses, and the primary intent of the study (ie, to compare outcomes in private for-profit vs private not-for-profit dialysis facilities or other). Reviewers resolved disagreements by consensus using the process described earlier. Our overall agreement was 98% for data abstraction. We successfully contacted all authors to obtain missing data, and in all instances authors were able to provide all the information we requested.

Data Synthesis

Prior to undertaking this study, we considered it appropriate to adjust for the following factors: age, sex, race, income, education, cause of end-stage renal disease (eg, diabetes, hypertension, chronic glomerulonephritis), comorbid conditions (eg, cancer, congestive heart failure, coronary artery disease), number of years receiving dialysis, market share of the dialysis facility (ie, competition), and whether the dialysis facility was part of a multinational chain corporation. We considered it ideal if measurement of these factors, particularly comorbid conditions that could result from suboptimal dialysis (eg, hypertension), was undertaken when patients initiated dialysis treatments. We considered analyses to be overadjusted if the investigators adjusted for variables that were under the control of the facility administrators, could be influenced by profit status, and could possibly affect mortality. These variables included hemoglobin or hematocrit levels after June 1989 (when Medicare authorized reimbursement for erythropoietin[11]), duration of dialysis treatments, staffing levels (ie, number of staff per dialysis treatment), skill level of the dialysis staff (eg, aids/technicians vs registered nurses), quality of equipment, and reuse of dialyzers.

Our quality assessment of studies included whether the study appropriately adjusted for any of the factors listed herein and avoided overadjustment as described, as well as identification of the source of data (data from individual chart reviews was considered superior to data from administrative databases).

Prior to the analysis, we specified several hypotheses to explain variability (ie, heterogeneity) in the direction and magnitude of effect among studies. We hypothesized that the effect size may differ based on whether the primary intent of the study was to compare outcomes in private for-profit vs private not-for-profit dialysis facilities; whether the study was restricted to dialysis facilities that were freestanding, hospital-based, or included both types of institutions; whether there was adjustment for market competition; whether there was overadjustment for the variables described; and whether we had to compute a corrected relative risk (RR) using the methods proposed by Zhang and Yu (Box).[12]

Box. Computation of Relative Risks (RRs)

Only 1 of the studies included in our systematic review directly provided an RR.[22] For the other studies, we had to convert some other measure of effect size to RR.

For 3 studies,[16,20,21] we generated estimates of 2×2 (profit status $\times$ mortality) tables and used these to estimate ln(RR) and its variance. Plough et al[16] reported information that enabled us to generate five 2×2 tables, 1 for each severity group. We used these tables to calculate an RR of 1-year mortality (private for-profit [PFP] relative to private not-for-profit [PNFP]) for each severity group; we then calculated a pooled estimate for the study using a meta-analytic method.[13] Irvin[20] reported a risk difference of 5.86%. McClellan et al[21] provided a linear regression analysis from which we were able to infer a risk difference of 0.73%. For these studies, we generated patient-level 2×2 tables consistent with those risk differences.

The study by Garg et al[18] used a Cox proportional hazards model with patient as the unit of analysis. In this case, we computed the RR at 1 year, using the following formula:

$$\text{RR at 1 Year} = \frac{1 - e^{HR \cdot \ln(1 - p_{PNFP})}}{p_{PNFP}}$$

where HR = hazard ratio (PFP relative to PNFP) and p_{PNFP} = death in PNFP units at 1 year.

Farley[17] and the 2 remaining studies by Irvin[19,23] used logistic regression, with patient as the unit of analysis. Because the death rates were greater than 10%, we could not use the coefficient for PFP relative to PNFP status as an estimate of ln(RR) because this can "exaggerate a risk association or treatment effect."[12] Therefore, we computed the corrected RR (and confidence interval) using the method of Zhang and Yu,[12] which yields an estimate that better represents the true RR:

$$\text{Corrected RR} = \frac{OR}{(1 - P_0) + (P_0 \times OR)}$$

where P_0 is the proportion of PNFP patients who died. P_0 was reported by Farley (19%),[17] but for Irvin's studies,[19,23] we had to use the overall proportions of patients who died (32.6% for Irvin[19]; 28.3% for Irvin[23]) as estimates of P_0. These were overestimates, so the corrected RRs we used are conservative (ie, closer to a value of 1 than they would be with the correct proportions).

Two of our RR estimates are derived from analyses that were not reported in the original studies. We report these estimates for McClellan et al[21] and Port et al[22] based on models with public hemodialysis facilities excluded. In the latter case,[22] profit status also had to be added to the model.

For each study, we computed the RR of mortality in private for-profit dialysis centers relative to private not-for-profit dialysis centers. Two independent reviewers blinded to the study results selected studies to pool in our primary pooled analysis on the basis of the following criteria: studies in which patients were likely to be included twice had to be separated in their time of enrollment by at least 2 years. For example, if one study completed enrollment on January 1, 1990, the next study could not begin enrolling before 1992. The purpose of this criterion was to limit the extent to which 2 studies used results from the same patients. If studies did have overlapping enrollment as described, the reviewers chose the largest study that adjusted for age, sex, race, and comorbidity (including diabetes). The reviewers independently agreed on which studies to pool in the primary meta-analysis.

We pooled these RRs using a random-effects model[13] and tested for heterogeneity using a χ^2 test. Data management and analysis were performed using SPSS software, version 11 (SPSS Inc, Chicago, Ill), and a meta-analysis program written by one of the authors (B.W.). We conducted a visual examination of funnel plots for evidence of publication bias.[14,15]

RESULTS

We identified 7 publications reporting 8 observational studies that met our eligibility criteria.[16-23] We also identified 12 publications that we believed might be eligible but required further information and/or data from the authors. After successfully contacting all authors, we confirmed that the majority of these studies had grouped private not-for-profit and public dialysis facilities together and that the authors either no longer had the data or could not rerun the analyses excluding the public institutions; these studies were excluded from our systematic review (TABLE 1).[24-35]

TABLE 2 presents the study characteristics and TABLE 3 presents the study methods of the 8 observational stud-

ies included in our systematic review. Table 3 lists the variables adjusted for in the analysis of each individual study. We successfully contacted all authors to clarify and obtain missing information. All studies were conducted in the United States and included data from January 1, 1973, through December 31, 1997. Three of the studies assessed only freestanding facilities and the remaining 5 evaluated both freestanding and hospital-based dialysis centers. The 8 studies included more than 500 000 patient-years of data and assessed a median of 1342 facilities per study. The most common duration of patient follow-up was 1 year.

Our quality assessment of studies revealed that all studies appropriately adjusted for many important determinants of mortality (including age, race, and cause of end-stage renal disease), 2 studies had overadjustments (including staffing levels and skill levels),[17,21] and only 1 study obtained data from patient charts.[18]

Six studies showed a statistically significant increase in adjusted mortality in for-profit facilities,[17-20,22,23] 1 showed a nonsignificant trend toward increased mortality in for-profit facilities,[21] and 1 showed a nonsignificant trend toward decreased mortality in for-profit facilities (FIGURE 2).[16]

Our primary meta-analysis pooled 4 studies and demonstrated that private for-profit dialysis centers were associated with an increased risk of death (RR, 1.08; 95% CI, 1.04-1.13; $P<.001$) that, with the exception of 1 study, was highly consistent across studies ($P=.08$ for heterogeneity) (Figure 2).[16,17,19,22] None of our predefined hypotheses to explain potential sources of heterogeneity demonstrated a statistically significant difference between the subgroup summary estimates. One study by Plough et al[16] completely confounded profit status with whether facilities were freestanding or hospital-based (ie, the investigators compared private for-profit freestanding facilities with private not-for-profit hospital centers). For several reasons (see "Comment"), this very different study

design could explain the difference in results across studies. The difference between the estimate of effect by Plough et al (RR, 0.71; 95% CI, 0.49-1.02)[16] and those of the other 3 studies (RR, 1.09; 95% CI, 1.07-1.11)[17,19,22] was statistically significant ($P=.02$). In the 3 unconfounded studies, the increased RR of 1.09 for mortality associated with care in a for-profit facility was significant ($P<.001$) and consistent ($P=.50$ for heterogeneity).[17,19,22]

We undertook 2 other sensitivity analyses that we planned a priori. Pooling the results of all 8 studies demonstrated that private for-profit dialysis facilities were associated with an increased risk of death (RR, 1.09; 95% CI, 1.05-1.12; $P<.001$; $P=.004$ for heterogeneity). Pooling the 3 studies that had restricted evaluation to freestanding dialysis units also demonstrated a statistically significant higher risk of death in private for-profit dialysis centers (RR, 1.11; 95% CI, 1.02-1.21; $P=.02$; $P=.004$ for heterogeneity).[18,20,23] Funnel plots did not suggest publication bias.

COMMENT
Principal Findings

Our systematic review identified 8 studies that assessed adjusted mortality rates of hemodialysis patients in private for-profit and private not-for-profit dialysis centers. Six of the studies demonstrated a statistically significant increased risk of death in private for-profit dialysis facilities. Approximately 20% to 25% of US in-center hemodialysis patients die each year,[36] and our meta-analysis found a pooled RR of death of 8%, suggesting that private for-profit dialysis facilities may be responsible for a substantial number of excess deaths.

Strengths and Weaknesses of This Review

We are unaware of any prior systematic reviews or meta-analyses that have compared mortality rates of hemodialysis patients in private for-profit and private not-for-profit dialysis facilities. We undertook a very broad search to identify studies for our systematic

Table 1. Excluded Publications Initially Thought to Be Possibly Eligible*

Source	Study Characteristics	Study Findings
Held et al,[24] 1987	This US study evaluated 4661 patients starting dialysis in 1977 and followed them until 1981. One analysis compared mortality in freestanding PFP and NFP (ie, both private and public) centers. When contacted, the authors were unable to repeat the analysis excluding the public institutions.	The patients in either PFP or NFP freestanding units had lower mortality (adjusted RRs, 0.88 and 0.78, respectively) than did patients in hospital centers. The difference between freestanding PFP and NFP favored lower mortality in the NFP centers, but the difference was not statistically significant.
Schlesinger et al,[25] 1989	This US study in 1981 of ESRD patients in 1050 facilities evaluated the outcomes of patients receiving kidney transplantation, hemodialysis, and peritoneal dialysis. The authors also established whether patients were receiving care at PFP, PNFP, or public facilities. They did not report the mortality rates for the various facilities and, when contacted, were unable to undertake this analysis.	No information presented or available to compare mortality rates in PFP and PNFP dialysis facilities.
Held et al,[26] 1988	This US study undertaken in 1981-1985 among 14 721 patients evaluated the effect of patient and dialysis unit characteristics (of which profit status was included) on access to kidney transplantation. Patient data was censored at death but the RR of death in the PFP and NFP centers was not reported. When contacted, the authors were unable to undertake an analysis of mortality rates in the PFP and PNFP facilities.	No information presented or available to compare mortality rates in PFP and PNFP dialysis facilities.
Held et al,[27] 1990	This US study included 14 807 patients who began hemodialysis in 1984 and were followed until 1987. This study compared the risks of mortality in PFP and NFP dialysis centers. When contacted, the authors were unable to undertake an analysis that excluded public facilities.	The patients in the PFP dialysis centers had a very small, nonsignificant increase in RR of mortality (adjusted RR, 1.01; $P = .82$) than the NFP dialysis centers.
Held et al,[28] 1991	This US study followed 600 patients who began hemodialysis (including home dialysis) in 1984 and were followed until 1987. Mortality rates with respect to profit status were not reported, and, when contacted, the authors were unable to undertake an analysis excluding public institutions and home hemodialysis patients.	No information presented or available to compare mortality rates in PFP and PNFP dialysis facilities.
Held et al,[29] 1994	This US study followed hemodialysis patients in freestanding dialysis centers for a year in 1989 and 1990. The total number of patients followed was 66 097. The authors had data on the profit status of the units but did not report a comparison between units. When contacted, the authors were unable to undertake an analysis of mortality rates in PFP and PNFP facilities.	No information presented or available to compare mortality rates in PFP and PNFP dialysis facilities.
Collins et al,[30] 1998	This US study followed hemodialysis patients receiving care at dialysis centers that practiced conventional dialysis (ie, <25% of patients with high-efficiency/high-flux dialysis). This article included 5 consecutive prevalent period cohorts from 1989-1993 that were divided into 2 study populations: 1989-1990 (10 357 patients) and 1991-1993 (13 551 patients). One of the analyses compared mortality in freestanding PFP and NFP centers and hospital PFP and NFP centers. When contacted, the authors were unable to repeat the analysis excluding public institutions.	Patients in hospital-based PFP units had significantly lower adjusted mortality rates than patients in hospital-based NFP units flux for both periods (1989-1990: RR, 0.86; 95% CI, 0.74-0.99; 1991-1993: RR, 0.70; 95% CI, 0.62-0.80). However, patients in freestanding PFP units had significantly higher adjusted mortality rates than patients in freestanding NFP units for both periods (1989-1990: RR, 1.38; 95% CI, 1.16-1.63; 1991-1993: RR, 1.16; 95% CI, 1.02-1.32). The results were overadjusted for reuse of dialyzers.
USRDS,[31] 1996	This study followed all US hemodialysis patients in freestanding PFP and NFP dialysis centers for 1 year in 1991, 1992, and 1993. Units with fewer than 20 expected first admissions were excluded. When contacted, the individuals who undertook the original analyses were unable to analyze mortality rates in PFP and PNFP facilities.	The study reported a statistically significant lower adjusted mortality rate in freestanding NFP units compared with freestanding PFP units (SMR in NFP units, 0.95; SMR in PFP units, 1.00).
Ebben et al,[32] 2000	This study followed all US hemodialysis patients who were alive during the last 6 months of an entry year from 1991-1995. Patients had to have >4 erythropoietin claims during the entry period. Patients were followed for 1 year and reported as 5 separate cohorts from 1992-1996. One of the analyses compared mortality rates in PFP and NFP centers. When contacted, the authors were unable to repeat the analysis excluding public institutions.	All 5 cohorts demonstrated lower adjusted mortality rates in NFP units compared with PFP units. The difference was statistically significant in 3 of the cohorts (1992, 1993, and 1994).
USRDS,[33] 1997	This study followed all US hemodialysis patients in freestanding PFP and NFP dialysis centers for 1 year in 1993, 1994, and 1995. Units with fewer than 20 expected first admissions were excluded. When contacted, the individuals who undertook the original analyses were unable to analyze mortality rates in PFP and PNFP facilities.	The study reported a statistically significant lower adjusted mortality rate in freestanding NFP units compared with freestanding PFP units (SMR in NFP units, 0.94; SMR in PFP units, 1.01).
Port et al,[34] 2001	This study followed 12 791 hemodialysis patients in 1394 dialysis facilities. Patients were followed in 1994-1995 in hospital-based freestanding PFP and freestanding NFP dialysis facilities. When contacted, the authors were unable to repeat the analysis excluding public institutions.	The authors reported no statistically significant difference in adjusted mortality rates between PFP and NFP units (numbers were not provided). The analysis was overadjusted for reuse of dialyzers.
McCullough et al,[35] 2001	This US study consisted of a random sample of 7956 patients selected from freestanding PFP (96) and NFP (15) and hospital-based NFP (33) units. Patients were followed from 1997-2000. When contacted, the authors were unable to repeat the analysis excluding public institutions.	The comparison of freestanding PFP and NFP units had a nonsignificant trend that favored longer survival in the PFP units (HR, 1.12; 95% CI, 0.94-1.33). The comparison of freestanding PFP and hospital-based NFP units also had a nonsignificant trend that favored longer survival in the PFP units (HR, 1.08; 95% CI, 0.96-1.21). The later analysis had completely confounded profit status with whether the facility was freestanding or hospital-based.

*PFP indicates private for-profit status; NFP, not-for-profit status, including both private and public institutions; RR, relative risk; ESRD, end-stage renal disease; PNFP, private not-for-profit status; CI, confidence interval; USRDS, US Renal Data System; SMR, standardized mortality ratio; and HR, hazard ratio.

review. We masked study results prior to determining study eligibility. We conducted all review procedures in duplicate and demonstrated a high degree of agreement in our eligibility decisions, data abstraction, and meta-analysis decisions. Our search identified 8 eligible observational studies with large sample sizes. We were successful in confirming and obtaining information from authors. In summary, our systematic review of these observational studies is methodologically rigorous[37] and transparently reported.[38]

Our systematic review has several limitations. We did not identify any randomized controlled trials. However, since it is unlikely that patients will ever be randomized to private for-profit and private not-for-profit health care delivery systems, the large studies in our systematic review represent the strongest feasible study design (ie, observational studies with adjustment for potential confounders) for answering our question. All included studies adjusted for age, race, and cause of end-stage renal disease. The last variable also provided some adjustment for comorbidity (eg, diabetes and hypertension).

Adjustment based on data from administrative databases is limited by the comprehensiveness and quality of the data. Careful data abstraction from individual patient charts represents a superior approach to account for important clinical confounders, particularly related to comorbidity. Only 1 study used data abstracted from individual patient charts; this study demonstrated the largest increase in mortality (RR increase of 18%).[18]

Another limitation of our systematic review was that in studies that combined private not-for-profit facilities with public facilities, many authors either did not have the data any longer or could not rerun analyses without data from the public dialysis facilities. However, 2 authors did rerun their analyses to remove the public institutions, and the results strengthened our systematic review.[21,22]

Pooling data from private not-for-profit and public dialysis centers is questionable. Theoretical reasons for potential differences in outcomes between public hospitals and private not-for-profit hospitals that provide dialysis include the public hospitals' funding

disadvantage and the possibility that public hospitals use some of the funds they receive for dialysis to help subsidize the care of other patients within their institutions.

For those who consider it appropriate to pool private and public not-for-profit institutions, the results of the majority of studies that combined these 2 types of facilities support the results of our systematic review. Seven of these 13 studies (including 2 very large US Renal Data System [USRDS] studies) demonstrated a statistically significant lower risk of death in not-for-profit dialysis centers compared with private for-profit centers,[30-33] and 4 demonstrated a trend favoring not-for-profit centers (Table 1).[24,27,32] In contrast, only 2 of these 13 studies demonstrated a statistically significant lower risk of death in patients receiving dialysis care in private for-profit hospitals compared with not-for-profit hospitals,[30] and 2 others demonstrated trends in favor of for-profit facilities (Table 1).[35] The 1 publication with 2 studies that showed a statistically significant result in favor of for-profit facilities was restricted to

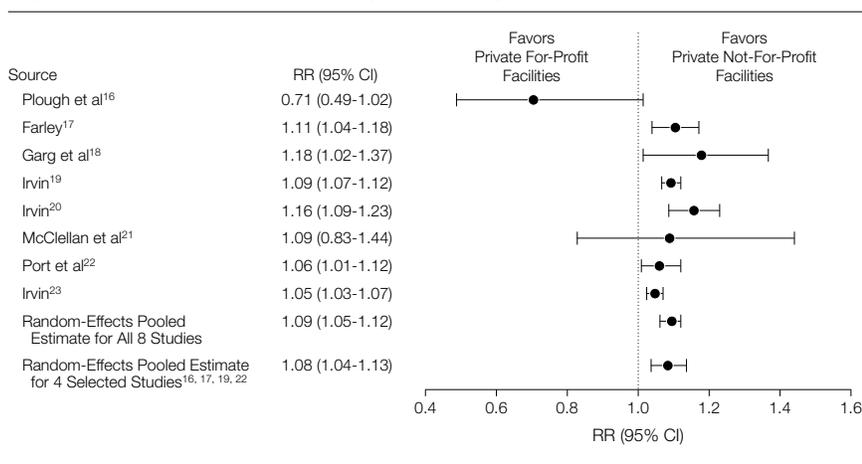**Table 2.** Characteristics of Studies Included in the Systematic Review*

Source	Type of Dialysis Center	Date of Data Collection		Follow-up Period for Individual Patients	No. of Dialysis Centers		Total No. of Patients Evaluated	
		Begun	Completed		PFP	PNFP	PFP	PNFP
Plough et al,[16] 1984	Freestanding PFP and hospital-based PNFP	1/1/73	12/31/82	1 Year	5	29	307	3135
Farley,[17] 1993	Freestanding and hospital-based PFP and PNFP	1/1/90	12/31/90	1 Year	946	656	43 395	26 008
Garg et al,[18] 1999	Freestanding PFP and PNFP	12/31/90 (First cohort); 12/31/93 (second cohort)	5/31/96	3-6 Years	574	86	2168	336
Irvin,[19] 1988	Freestanding and hospital-based PFP and PNFP	1/1/93	12/31/93	1 Year	1432	769	106 592	52 601
Irvin,[20] 1988	Freestanding PFP and PNFP	1/1/93	12/31/93	1 Year	944	137	13 481	1941
McClellan et al,[21] 1998	Freestanding and hospital-based PFP and PNFP	10/1/94	4/30/95	7 Months	169	28	4647	770
Port et al,[22] 2000	Freestanding and hospital-based PFP and PNFP	1/1/95	12/31/97	1-2 Years	1988	856	60 421	28 024
Irvin,[23] 2000	Freestanding PFP and PNFP	1/1/96	12/31/96	1 Year	1934	264	151 967	28 946

*PFP indicates private for-profit status; PNFP, private not-for-profit status.

Table 3. Methods of Studies Included in the Systematic Review*

Source	Sampling Method	Data Source	Factors Controlled for in Analysis
Plough et al,[16] 1984	All patients in a registry who began hemodialysis between 1973 and 1981 in any of 34 Michigan dialysis treatment centers. Patients with acute reversible renal failure, who were not in 1 facility for 120 days, or who did not survive for 120 days after starting hemodialysis were excluded.	Michigan Kidney Registry.	Age, race, primary renal diagnosis (ie, hypertension, diabetes mellitus, chronic glomerulonephritis, and chronic interstitial nephritis), and comorbid conditions (ie, cancer, collagen disease, pulmonary disease, vascular disease, social/behavioral disorder, and heart disease).
Farley,[17] 1993	All hemodialysis patients who began 1990 as ESRD patients in any US Medicare-certified ESRD facility that provided hemodialysis services. Facilities were excluded if many of their patients were temporary out-of-state patients or if the facility began or closed operation in 1990. Patients undergoing kidney transplantation in 1990 were excluded.	Medicare Program Management and Medical Information System, annual ESRD facility survey data, census data.	Age, sex, race (ie, African American, Asian, Native American, or other), diabetes, hypertension, other ESRD causes, unknown cause of ESRD, failed transplant, years with ESRD, market share (ie, the power an individual provider has relative to other providers serving its market), patient transfer rate (ie, the rates at which patients change dialysis providers), hospital-based centers, and number of hemodialysis stations. Patient primary providers were identified as the dialysis facility that provided the greatest fraction of a patient's total treatment. The results are overadjusted for treatments/staff hours and staff hours for licensed practical nurses, aids, and technicians/nursing staff.
Garg et al,[18] 1999	Patients with newly diagnosed ESRD receiving hemodialysis in a PFP or PNFP freestanding dialysis facility were selected from 2 nationally representative cohorts. Facilities were systematically sampled at a national level to ensure representation with regard to the ESRD network, distance from the network office, and size. Patients who were followed for <90 days and patients for whom data were missing for more than half the clinical variables were excluded. Patients also had to be >20 years old and have had their first dialysis in the initial year of each cohort study.	Data were abstracted from patient charts in both cohort studies (the Case-Mix Adequacy cohort and Wave 1 cohort). Data were also obtained from the USRDS.	Age, race, high school diploma, year of onset of ESRD, primary cause of ESRD, residence in a nursing home, current smoking status, body mass index, dependence on others for assistance with activities of daily living, serum albumin concentration, and presence or absence of cancer, cardiomyopathy, cerebrovascular disease, congestive heart failure, coronary artery disease, chronic obstructive pulmonary disease, diabetes, hypertension, and peripheral vascular disease at onset of ESRD. Longitudinal data were used to identify changes in patients' providers and included the type of facility as a time-dependent covariate. There was also correction for clustering according to facility.
Irvin,[19] 1988	All US patients receiving hemodialysis at a PFP or PNFP freestanding or hospital-based dialysis facility and receiving Medicare benefits as of December 31, 1992. Patients <65 years old had to have been receiving hemodialysis for ≥3 months.	USRDS database, US census. Data on certificate of need were obtained from the National Directory of Health Planning, Policy and Regulatory Agencies.	Age, sex, race (ie, Native American, black, Asian, or other nonwhite), income, education, urban location, region, days receiving dialysis, primary diagnosis causing ESRD (ie, diabetes, hypertension, glomerulonephritis, or cystic kidneys), freestanding facility, level and nature of competition in the market as indicated by the presence of certificate-of-need regulations and the Hirschman-Herfindahl index, and monopoly power of a firm in a market as measured by the market share variable. Some patients were treated at >1 facility in 1993. Data were used from the facility where the patient was treated for the longest period.
Irvin,[20] 1988	All US patients receiving hemodialysis at a PFP or PNFP freestanding dialysis facility who were black or white, had diabetes or hypertension, and received Medicare benefits as of December 31, 1992. Patients <65 years old had to have been receiving hemodialysis for ≥3 months.	USRDS database, US census. Data on certificate of need were obtained from the National Directory of Health Planning, Policy and Regulatory Agencies.	Unlike the other studies, this study does not report results from a multivariate analysis. Rather, patients were matched for factors demonstrated to be associated with mortality: age, sex, race (ie, black), household income, average years of school, days receiving dialysis, diabetes, South region, and certificate of need. Some patients were treated at >1 facility in 1993. Data were used from the facility where the patient was treated for the longest period.
McClellan et al,[21] 1998	Random sample of hemodialysis patients from all PFP and PNFP hemodialysis facilities in North Carolina, South Carolina, and Georgia.	Facility survey and ESRD Network data.	Age, sex, race, cause of renal failure, functional status as assessed by center staff according to a modified Karnofsky scale, serum albumin concentration, history of angina pectoris, myocardial infarction, congestive heart failure, and freestanding facilities. Patients were censored at the time of transplantation, transfer from the treatment center, or the end of the study. The results were overadjusted for mean urea reduction ratio and physician visits (at least once per week).
Port et al,[22] 2000	All US patients who began receiving hemodialysis in 1995 or 1996 at all PFP and PNFP facilities.	USRDS data.	Age, sex, race, cause of ESRD, geographic region, alcohol dependence, cancer, cardiac arrest, myocardial infarction, ischemic heart disease, congestive heart failure, stroke, transient ischemic attack, diabetes, current insulin therapy, drug dependence, cardiac dysrhythmia, history of hypertension, inability to ambulate, inability to transfer, pericarditis, chronic obstructive pulmonary disease, peripheral vascular disease, and current smoking status. Clustering of patients was accounted for and patient data were censored when they underwent transplantation.
Irvin,[23] 2000	All US patients who had been receiving hemodialysis for ≥3 months or were >65 years old at the start of hemodialysis at a PFP or PNFP freestanding dialysis facility. Patients also had to be receiving Medicare benefits as of December 31, 1995.	USRDS database, US census. Data on certificate of need were obtained from the National Directory of Health Planning, Policy and Regulatory Agencies.	Age, sex, race, income, education, urban location, region, days receiving dialysis, primary diagnosis causing ESRD, and level and nature of competition in the market as indicated by the presence of certificate-of-need regulations. Some patients were treated at >1 facility in 1996. Data were used from the facility where the patient was treated for the longest period.

*ESRD indicates end-stage renal disease; PFP, private for-profit status; PNFP, private not-for-profit status; and USRDS, US Renal Data System.

Figure 2. Relative Risk (RR) of Mortality in Hemodialysis Patients

Source	RR (95% CI)	Favors Private For-Profit Facilities	Favors Private Not-For-Profit Facilities
Plough et al[16]	0.71 (0.49-1.02)		
Farley[17]	1.11 (1.04-1.18)		
Garg et al[18]	1.18 (1.02-1.37)		
Irvin[19]	1.09 (1.07-1.12)		
Irvin[20]	1.16 (1.09-1.23)		
McClellan et al[21]	1.09 (0.83-1.44)		
Port et al[22]	1.06 (1.01-1.12)		
Irvin[23]	1.05 (1.03-1.07)		
Random-Effects Pooled Estimate for All 8 Studies	1.09 (1.05-1.12)		
Random-Effects Pooled Estimate for 4 Selected Studies[16, 17, 19, 22]	1.08 (1.04-1.13)		

RR (95% CI): 0.4 0.6 0.8 1.0 1.2 1.4 1.6

hospitals. Furthermore, they were the only 2 studies that restricted their samples to dialysis units with less than 25% of patients with high-efficiency/high-flux dialysis, and included an overadjustment for reuse of dialyzers.[30]

Although formal tests of heterogeneity may lack power, aside from 1 study by Plough et al,[16] the results of eligible studies are very consistent (Figure 2), strengthening the inferences from this systematic review. The results of Plough et al raise challenges in interpretation because profit status was completely confounded with hospital and freestanding facilities (the authors compared private for-profit freestanding facilities with private not-for-profit hospital-based centers). Hospital-based hemodialysis may be associated with higher mortality than dialysis in freestanding facilities, irrespective of profit status.[24]

Significance of This Systematic Review

Our systematic review demonstrated an increased risk of death in private for-profit dialysis centers (RR, 1.08; 95% CI, 1.04-1.13). Several studies have demonstrated mechanisms through which this increased risk of death may be occurring. Studies (including 1 in our systematic review) have demonstrated that private for-profit dialysis centers employ fewer personnel per dialysis run and less-highly skilled personnel (ie, more licensed practical nurses, aids, and technicians compared with registered nurses).[17,27,39] Other studies have also demonstrated that patients at private for-profit dialysis facilities have shorter durations of dialysis treatment.[27,28] Shorter durations of dialysis treatment are associated with higher mortality.[27,28]

In a health care system in which funding is relatively fixed, as with dialysis care in the United States, the private for-profit facilities face a difficult economic challenge. Shareholders expect 10% to 15% returns on their investments[3] and taxes may account for 5% to 6% of total expenses.[40] Private for-profit facilities must generate these profits and pay taxes while endeavoring to provide the same quality care as private not-for-profit centers that are free of these expenses. Given that nurse and technician wages account for approximately 70% of total dialysis costs, it is understandable that private for-profit centers may try to minimize staff and the skill (and, thus, reimbursement) level of staff.[17,27,39]

How many deaths might realistically be avoided if private not-for-profit facilities delivered all dialysis care in the United States? There are approximately 208 000 patients receiving incenter hemodialysis in the United States each year, of whom approximately 75% receive their dialysis in for-profit facilities.[9] Making a conservative esti-

mate of the proportion who die each year, 20%,[36] and using our pooled estimate of an 8% (95% CI, 4%-13%) relative increase in mortality in for-profit facilities, one can estimate that were these patients to receive their dialysis in private not-for-profit facilities, approximately 2500 deaths (range, 1200-4000) could be avoided each year.

Many countries face choices about the optimal methods of health care delivery. For instance, Canada is currently undergoing intense debate concerning the relative merits of private for-profit vs private not-for-profit health care delivery. Our results suggest the inadvisability of introducing private for-profit dialysis centers into the Canadian health care system.

A previous systematic review suggested that private for-profit hospitals increase mortality relative to private not-for-profit hospitals.[10] Together with the results of this review, these data provide compelling evidence that profit status can have an important impact on the outcomes of medical care.

dertook the searches involved in this study. We thank P. J. Held, PhD, and J. M. Soucie, PhD, for their assistance with the relative risk analyses. We also thank all of the authors of the included studies who confirmed information, provided information, and performed additional analyses for our systematic review.

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by the programs that we studied did use diagnosis data to identify drug-disease interactions, and those deciding which exceptions should result in alerts did have access to patient-specific factors such as those mentioned by Berringer et al. We agree that the low alert rate that we found could well explain a lack of effect, as we stated in our article, but this reflects how such programs were implemented. Furthermore, we did not find a dose-response relationship with numbers of alerts.

The articles cited by Berringer et al as evidence of the effectiveness of such programs deserve clarification. The study by Monane et al[1] examined a prospective rather than a retrospective drug utilization review program, and both studies cited[1,2] lacked control groups, seriously limiting their interpretability. There are a few controlled studies suggesting that mailed alert letters can affect prescribing in a modest subset of the patients who are identified in alerts.[3,4] However, the only study previous to ours that examined clinical impact of retrospective drug utilization review also failed to show an effect.[5]

Like Berringer et al, Dr Christensen and colleagues wonder whether an effect would have been detectable given the low alert rate. The low alert rate was a finding that we had not anticipated at the outset of our study, and we discussed it as a likely factor in our results. This is not a weakness of our study, but rather a weakness of the programs. Examining outcomes in patients identified in alerts would have been problematic because of the lack of an appropriate control group. We did examine cause-specific hospitalizations following specific alerts in addition to all-cause hospitalization, and found no evidence for effect on these outcomes. Although we did not look specifically for harmful effects, unintended consequences of programmatic efforts are not uncommon, and retrospective drug utilization review programs in particular might have unintended consequences.[4] Our study focused on measuring the effectiveness of the programs rather than evaluating process measures such as the content, quality, and response to alert letters.

We applaud recent efforts to improve retrospective drug utilization review programs, and hope that the improved programs will be evaluated rigorously. We believe, however, that widespread adoption of and legal requirements for such programs should await evidence that they are effective and are free of major unintended effects.

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CORRECTIONS

Incorrect Data: In the Editorial entitled "Suicide Risk and Treatments for Patients With Bipolar Disorder" published in the September 17, 2003, issue of THE JOURNAL (2003;290:1517-1519), incorrect data were reported. On page 1518, the second full sentence in the second column should have read, "The difference in risk without vs with lithium treatment was 1.8-fold (0.116/0.066), positive but lower than in previous experience (nearly 9-fold).[26]"

Patent Application: In the Original Contribution entitled "Association Between Estrogen Receptor α Gene Variation and Cardiovascular Disease" published in the November 5, 2003, issue of THE JOURNAL (2003;290:2263-2270), a provisional patent application was filed after the article went to press. The patent application for medical uses related to the *ESR1 c.454-397T>C* polymorphism was filed through the Massachusetts Institute of Technology's Technology Licensing Office on behalf of Drs Housman, Levy, Mendelsohn, and Shearman.

Incorrect Information: In the Review entitled "Comparison of Mortality Between Private For-Profit and Private Not-For-Profit Hemodialysis Centers" published in the November 20, 2002, issue of THE JOURNAL (2002;288:2449-2457), incorrect information was published. In Table 2 on page 2454, the years shown in the first column for Irvin[19-20] should have been 1998. Additionally, for the dissertation in references 19 and 20 on page 2457, the name and location of the university should have been University of Washington, Seattle.