Outpatient Talc Administration by Indwelling Pleural Catheter for Malignant Effusion


ABSTRACT

BACKGROUND
Malignant pleural effusion affects more than 750,000 persons each year across Europe and the United States. Pleurodesis with the administration of talc in hospitalized patients is the most common treatment, but indwelling pleural catheters placed for drainage offer an ambulatory alternative. We examined whether talc administered through an indwelling pleural catheter was more effective at inducing pleurodesis than the use of an indwelling pleural catheter alone.

METHODS
Over a period of 4 years, we recruited patients with malignant pleural effusion at 18 centers in the United Kingdom. After the insertion of an indwelling pleural catheter, patients underwent drainage regularly on an outpatient basis. If there was no evidence of substantial lung entrapment (nonexpandable lung, in which lung expansion and pleural apposition are not possible because of visceral fibrosis or bronchial obstruction) at 10 days, patients were randomly assigned to receive either 4 g of talc slurry or placebo through the indwelling pleural catheter on an outpatient basis. Talc or placebo was administered on a single-blind basis. Follow-up lasted for 70 days. The primary outcome was successful pleurodesis at day 35 after randomization.

RESULTS
The target of 154 patients undergoing randomization was reached after 584 patients were approached. At day 35, a total of 30 of 69 patients (43%) in the talc group had successful pleurodesis, as compared with 16 of 70 (23%) in the placebo group (hazard ratio, 2.20; 95% confidence interval, 1.23 to 3.92; P=0.008). No significant between-group differences in effusion size and complexity, number of inpatient days, mortality, or number of adverse events were identified. No significant excess of blockages of the indwelling pleural catheter was noted in the talc group.

CONCLUSIONS
Among patients without substantial lung entrapment, the outpatient administration of talc through an indwelling pleural catheter for the treatment of malignant pleural effusion resulted in a significantly higher chance of pleurodesis at 35 days than an indwelling catheter alone, with no deleterious effects. (Funded by Becton Dickinson; EudraCT number, 2012-000599-40.)
Malignant pleural effusion is estimated to affect more than 750,000 persons each year across Europe and the United States. Malignant pleural effusion is usually the result of the spread of metastatic cancer and commonly leads to debilitating symptoms and to multiple interventions as fluid recurs.

Historically, the preferred approach in the treatment of malignant pleural effusion has involved inducing pleurodesis, with recent data from a meta-analysis confirming that talc is likely to be the most efficacious agent for this process. The primary disadvantage of chemical pleurodesis is that it usually involves an inpatient stay of 4 to 7 days that, in patients receiving palliative treatment for malignant pleural effusion, may represent a substantial proportion of a patient’s remaining life.

Indwelling pleural catheters offer an ambulatory alternative for fluid management and are now routinely inserted as day-case procedures (i.e., with the intervention and discharge occurring on the same day). Used in isolation, these catheters have been shown to be as good as traditional approaches in managing symptoms in patients, but they do not confer the same likelihood of pleurodesis, although pleurodesis has been reported to happen spontaneously at rates as disparate as 16% and 65% among patients with malignant pleural effusion.

In a noncomparative series involving 22 patients, the administration of talc through an indwelling pleural catheter suggested that high rates of pleurodesis were achievable. In the present trial, we tested the hypothesis that a combination of talc and indwelling pleural catheter would enhance the probability of successful pleurodesis, as compared with the use of an indwelling pleural catheter alone.

Methods

Trial Design

The IPC–Plus trial was a randomized, placebo-controlled, single-blind, parallel-group trial. The trial was supported by an unrestricted research grant from Becton Dickinson, which also supplied PleurX catheters and drainage bottles for all the participants. The trial design, implementation, and data collection and analysis were performed solely by the trial investigators without commercial involvement. The authors wrote the manuscript and made the decision to submit it for publication without commercial involvement. The authors vouch for the accuracy and completeness of the data and for the fidelity of the trial to the protocol (available with the full text of this article at NEJM.org).

North Bristol NHS Trust provided trial oversight. Ethics approval for recruitment was obtained from the South Central (Oxford A) Research Ethics Committee and from the Medicines and Healthcare Products Regulatory Agency. Details regarding trial oversight are provided in the Supplementary Appendix, available at NEJM.org.

Trial Setting and Participants

The trial recruited patients from 18 secondary and tertiary care centers in the United Kingdom. Potential participants were identified and screened at local centers offering routine pleural services. Patients were eligible if they had a confirmed diagnosis of symptomatic malignant pleural effusion for which the patient had elected treatment with an indwelling pleural catheter. In addition, participants had to have an expected survival of more than 2 months (as judged by a local investigator) and an expected Eastern Cooperative Oncology Group performance-status score of 2 or less (on a scale from 0 to 4, with higher scores indicating greater disability) after fluid removal. Key exclusion criteria were an age younger than 18 years, extensive lung entrapment (nonexpandable lung, in which lung expansion and pleural apposition are not possible because of visceral fibrosis or bronchial obstruction) or fluid loculation, ipsilateral attempt at pleurodesis within the previous 8 weeks, and any contraindication to the trial procedures (see the Supplementary Appendix).

Enrollment, Randomization, and Blinding

All the participants provided written informed consent. After enrollment, patients underwent insertion of an indwelling pleural catheter while they were under local anesthesia; maximal fluid drainage occurred at the time of catheter placement, as limited by symptoms. Patients were discharged home the same day, and a minimum of three further drainages, limited to 1 liter each, took place before review at day 10 after the insertion of the catheter. Drainage took place at home.
with the assistance of a community nurse or at an outpatient clinic or trial center. Participants then underwent maximal drainage once more at a trial center before undergoing radiography of the chest. On the basis of visual estimation, patients who had evidence of less than 75% pleural apposition on a radiograph of the chest or who had more than one third opacification due to fluid (as estimated with the use of thoracic ultrasonography) were considered to be ineligible.

Participants underwent randomization with the use of a centralized, computer-based system. Trial-group assignments were made in a 1:1 ratio, with the use of minimization\textsuperscript{11} with a random component of 80%. The minimization variables were the following: type of cancer (breast or ovarian cancer vs. mesothelioma vs. other), the total volume of pleural fluid drained between enrollment and randomization (<2 liters vs. ≥2 liters), and the appearance on the chest radiograph obtained at day 10 (no lung entrapment vs. some entrapment but the patient was still eligible for randomization).

The trial was conducted on a single-blind basis. Trial-group assignments were known only to the local clinical team, and talc or placebo was administered through the indwelling pleural catheter immediately after randomization. Participants remained unaware of their group assignment throughout the follow-up period. Community nurses who recorded the drainage volumes that were used to assess the primary outcome were also unaware of the trial-group assignments.

**Interventions**

According to standard clinical practice, all the participants received a dose of intrapleural lidocaine, adjusted for body weight, before the administration of talc or placebo. Patients in the placebo group received 50 ml of intrapleural sodium chloride 0.9% solution as a control material through the indwelling pleural catheter. Patients in the talc group received a U.K. guideline–recommended dose of 4 g of sterile, graded talc (Steritalc, Novatech),\textsuperscript{2} which had been made into a slurry before instillation with 50 ml of sodium chloride 0.9% solution. Although the two solutions were visibly distinct, participants remained unaware of the trial-group assignment owing to the use of opaque syringes and to the fact that talc or placebo was administered in a manner such that the patients could not see the procedure (see the Supplementary Appendix).

Participants were discharged after a 2-hour minimum period of observation, and the next drainage took place between 12 and 36 hours after the administration of talc or placebo. Subsequent drainage frequency was determined by the local investigating team but was at least twice per week for the duration of the trial.

**Follow-up**

Patients were followed for trial outcomes until 70 days after randomization or until death (whichever occurred first). Trial consultations took place every 14 days. The recording of maximal fluid drainage and radiography of the chest were undertaken immediately before face-to-face assessments, which were performed by members of the local trial teams. All decisions regarding a participant’s overall care, including whether to remove an indwelling pleural catheter, were at the discretion of the treating clinicians at each center.

**Primary Outcome**

The primary-outcome measure was the proportion of participants with successful pleurodesis at day 35 after randomization. Pleurodesis was declared to be a success if two objective criteria were met: if less than 50 ml of fluid was drained on three consecutive occasions through the indwelling pleural catheter; and if a radiograph of the chest that was taken after these drainages showed less than 25% opacification of the appropriate hemithorax due to suspected fluid. The interpretation of radiographs was performed by two independent pulmonologists who were unaware of the trial-group assignments (see the Supplementary Appendix).

**Secondary Outcomes**

Secondary outcomes included participant-reported health-related quality of life as measured with the use of the EuroQoL Group 5-Dimensions 5-Level Questionnaire\textsuperscript{12} (EQ-5D-5L; scores on the descriptive index range from −0.59 to 1.00, and scores on the visual-analogue scale range from 0 to 100, with higher scores indicating better quality of life) and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire–Core 30 (QLQ-C30)\textsuperscript{13} (the summary score ranges from 0 to 100, with a...
higher score indicating better quality of life; participant-reported dyspnea and chest pain as assessed by means of scores on a visual-analogue scale (on a scale from 0 to 100 mm, with a score of 0 indicating a complete absence of symptoms and a score of 100 maximum possible symptoms) that were recorded daily; the total volume of fluid drained between randomization and day 70; all-cause mortality up to day 70; the number of hospital inpatient days between randomization and day 70; the degree of pleural fluid complexity (septation or loculation) as assessed with the use of thoracic ultrasonography; successful pleurodesis at day 70 (defined identically to successful pleurodesis in the primary-outcome analysis); successful pleurodesis at both day 35 and day 70, defined as less than a total of 250 ml of fluid being drained over a 2-week period; and the number of therapeutic pleural procedures that took place between randomization and day 70. Details regarding all adverse events and deaths during the trial were assessed initially by the local investigator and were then verified independently by North Bristol NHS Trust, by the chief investigator, and finally by the data and safety monitoring committee. Details are provided in the Supplementary Appendix.

**STATISTICAL ANALYSIS**

Previous studies have shown rates of successful pleurodesis of approximately 90% among patients who received talc slurry by means of traditional methods and up to 65% among those who used an indwelling pleural catheter alone.8,14 Assuming a difference of at least 25 percentage points in the rates of participants who had successful pleurodesis at day 35 after randomization (85% in the talc group vs. 60% in the placebo group) and a 5% loss to follow-up, we calculated that 154 participants (with randomization performed in a 1:1 ratio) would be required for the trial to have 90% power at a 5% significance level.

Analyses were performed with the use of Stata software, version 12 (StataCorp). The main analysis for each outcome was performed according to the intention-to-treat principle; all the participants with an observed outcome were included in the analysis according to their assigned trial group.15 All the analyses used minimization variables as covariates in regression models.16,17 All the tests were two-sided, and results were considered to be significant at the 5% level.

The primary outcome was analyzed with the use of a competing-risk time-to-event regression model, with death as the competing risk.18 Participants who did not die or have the primary outcome had their data censored at day 35 after randomization or at the point of last contact.

The original statistical analysis plan stipulated that an interim analysis for efficacy would take place after the randomization of 100 participants and that a significance threshold of 0.048 was required at final analysis.19 However, after good recruitment of participants, the trial steering committee and data and safety monitoring committee recommended that the trial continue to its original target of 154 participants undergoing randomization, without an interim analysis being performed. The trial protocol and statistical analysis plan were therefore amended, and a P value of less than 0.05 was considered to indicate statistical significance (see the Supplementary Appendix).

**RESULTS**

**RECRUITMENT AND POPULATION CHARACTERISTICS**

Recruitment and follow-up of the participants took place over a period of 4 years, from June 2012 through December 2016. A total of 923 potential participants were assessed for entry, 584 were approached, and 307 were willing to consider enrollment. A total of 154 patients underwent randomization; 76 patients were assigned to the placebo group and 78 to the talc group, with 70 and 69 patients, respectively, contributing data to the intention-to-treat analysis of the primary outcome (Fig. 1). During the course of the trial, 20 participants withdrew (10 from each group). The two trial groups were generally well matched at baseline, although an imbalance was seen among patients who were being treated with low-molecular-weight heparin (Table 1, and Table S1 in the Supplementary Appendix).

**PRIMARY OUTCOME**

In the primary-outcome analysis, 30 of 69 patients (43%) in the talc group had successful pleurodesis by day 35, as compared with 16 of 70 (23%) in the placebo group (hazard ratio, 2.20; 95% confidence interval [CI], 1.23 to 3.92; P=0.008). All the sensitivity analyses, including those that were performed to address missing data and the baseline imbalance in treatment with low-molecular-weight heparin, favored a beneficial effect from talc. The prespecified sub-
923 Patients were assessed for eligibility

339 Did not meet criteria
- 153 Were unwell or had limited life expectancy
- 50 Had recent pleurodesis with talc
- 41 Had evidence of lung entrapment
- 28 Were unable to give consent
- 14 Had effusion that was too loculated
- 53 Had other or unknown reason

584 Met entry criteria

277 Declined trial entry
- 94 Preferred other treatment for malignant pleural effusion or other trial
- 91 Did not give reason
- 70 Were unable or unwilling to adhere to visit schedule
- 13 Were not interested in participating in research
- 6 Were not interested in participating in this trial
- 3 Did not want to receive talc

307 Were considered to be suitable for enrollment

57 Were excluded before enrollment
- 17 Received urgent treatment
- 4 Had conflict with other treatments
- 4 Had conflict with other clinical trial
- 32 Had other reason

250 Provided informed consent and were enrolled

96 Had run-in failure
- 32 Had substantial lung entrapment
- 23 Were too unwell
- 13 Had issue with indwelling pleural catheter (including no insertion)
- 8 Declined follow-up
- 6 Died before randomization
- 4 Withdrew
- 3 Had spontaneous pleurodesis
- 1 Was lost to follow-up
- 6 Had other reason

154 Underwent randomization

76 Were assigned to placebo group
- 6 Were excluded owing to insufficient data to calculate primary outcome at day 35
- 70 Were included in intention-to-treat analysis of primary outcome

78 Were assigned to talc group
- 9 Were excluded owing to insufficient data to calculate primary outcome at day 35
- 69 Were included in intention-to-treat analysis of primary outcome

Figure 1. Identification, Enrollment, Randomization, and Follow-up of the Patients.
group analyses did not reveal any significant differences in the effect with talc versus placebo (Fig. 2, and Tables S2 and S3 in the Supplementary Appendix).

**SECONDARY OUTCOMES**

**Additional Pleurodesis and Fluid-Drainage Outcomes**

The rate of successful pleurodesis (according to the primary-outcome definition) at day 70 was 51% (35 of 69 patients) in the talc group, compared with 27% (19 of 70 patients) in the placebo group (hazard ratio, 2.24; 95% CI, 1.31 to 3.85; \( P = 0.003 \)). The assessment of pleurodesis according to the total volume of fluid drained over a period of 2 weeks also favored the talc group over the placebo group at day 35 (28 of 67 patients [42%] vs. 9 of 70 [13%]; hazard ratio, 3.78; 95% CI, 1.81 to 7.90; \( P < 0.001 \)) and at day 70 (30 of 66 patients [45%] vs. 11 of 69 [16%]; hazard ratio, 3.43; 95% CI, 1.74 to 6.75; \( P < 0.001 \)).

### Table 1. Characteristics of the Patients at Baseline.\(^*\)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Placebo Group (N = 76)</th>
<th>Talc Group (N = 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age — yr</td>
<td>68.7±10.1</td>
<td>67.7±12.7</td>
</tr>
<tr>
<td>Female sex — no. (%)</td>
<td>39 (51)</td>
<td>44 (56)</td>
</tr>
<tr>
<td>ECOG performance-status score — no. (%)(^†)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>10 (13)</td>
<td>8 (10)</td>
</tr>
<tr>
<td>1</td>
<td>33 (43)</td>
<td>38 (49)</td>
</tr>
<tr>
<td>2</td>
<td>16 (21)</td>
<td>23 (29)</td>
</tr>
<tr>
<td>3</td>
<td>16 (21)</td>
<td>8 (10)</td>
</tr>
<tr>
<td>Missing data</td>
<td>1 (1)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Most common cancer types — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>25 (33)</td>
<td>20 (26)</td>
</tr>
<tr>
<td>Breast</td>
<td>16 (21)</td>
<td>15 (19)</td>
</tr>
<tr>
<td>Mesothelioma</td>
<td>10 (13)</td>
<td>13 (17)</td>
</tr>
<tr>
<td>Ovarian</td>
<td>5 (7)</td>
<td>6 (8)</td>
</tr>
<tr>
<td>Renal</td>
<td>4 (5)</td>
<td>5 (6)</td>
</tr>
<tr>
<td>Lung entrapment of &lt;25% at randomization — no. (%)</td>
<td>14 (18)</td>
<td>16 (21)</td>
</tr>
<tr>
<td>No. of pleural interventions in previous 3 mo</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>0–2</td>
<td>1–2</td>
</tr>
<tr>
<td>Treatment at baseline</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral glucocorticoid — no./total no. (%)</td>
<td>13/75 (17)</td>
<td>7/77 (9)</td>
</tr>
<tr>
<td>Nonsteroidal antiinflammatory drug — no./total no. (%)</td>
<td>14/75 (19)</td>
<td>11/77 (14)</td>
</tr>
<tr>
<td>Low-molecular-weight heparin — no./total no. (%)</td>
<td>12/72 (17)</td>
<td>4/75 (5)</td>
</tr>
<tr>
<td>Warfarin — no./total no. (%)</td>
<td>3/64 (5)</td>
<td>4/73 (5)</td>
</tr>
<tr>
<td>Radiotherapy — no./total no. (%)</td>
<td>14/75 (19)</td>
<td>19/78 (24)</td>
</tr>
<tr>
<td>Hormone therapy — no. (%)</td>
<td>9 (12)</td>
<td>7 (9)</td>
</tr>
<tr>
<td>Chemotherapy — no. (%)</td>
<td>6 (8)</td>
<td>15 (19)</td>
</tr>
</tbody>
</table>

\(^*\) Plus–minus values are means ±SD. A significant imbalance was noted in patients receiving anticoagulation therapy with low-molecular-weight heparin (\( P = 0.03 \)). No other baseline imbalances were identified. Percentages may not total 100 because of rounding. A comprehensive table of baseline characteristics is provided in Table S1 in the Supplementary Appendix.

\(^†\) The Eastern Cooperative Oncology Group (ECOG) performance-status scores range from 0 to 4, with higher scores indicating greater disability. Patients were expected to have a score of 2 or less after fluid removal.
The median volume of fluid that was drained between randomization and day 70 was 1350 ml (interquartile range, 340 to 5680) in the talc group and 3640 ml (interquartile range, 845 to 7605) in the placebo group (P=0.36). A total of 5 of 71 patients (7%) in the talc group underwent an additional therapeutic procedure for fluid management during the trial, as compared with 2 of 73 (3%) in the placebo group (odds ratio, 2.69; 95% CI, 0.50 to 14.34; P=0.25).

Quality of Life
Participants who received talc reported better quality-of-life scores than those who received placebo at all time points, with differences in the QLQ-C30 score reaching significance at day 28 (difference, 9.2 points; 95% CI, 1.1 to 17.4; P=0.03) and day 42 (difference, 14.7 points; 95% CI, 5.9 to 23.5; P=0.001) and differences in the EQ-5D-5L score reaching significance at day 42 only (difference, 0.12 points; 95% CI, 0.01 to 0.22; P=0.03). Post hoc analysis of mean scores over the whole trial showed that the difference in means for the QLQ-C30 score was 6.9 points (95% CI, 1.2 to 12.6; P=0.02) and the difference in means for the EQ-5D-5L score was 0.07 points (95% CI, 0.00 to 0.14; P=0.04).

Symptoms
Participants who received talc had better symptom scores at all assessment points during the trial, with significant differences in the mean scores on the visual-analogue scale for chest pain being seen at day 14 (difference, −5.4 points; 95% CI, −10.7 to −0.1; P=0.04) and day 28 (difference, −6.8 points; 95% CI, −12.6 to −0.9; P=0.02) and significant differences in the mean scores on the visual-analogue scale for dyspnea being seen at day 56 (difference, −7.9 points; 95% CI, −15.5 to −0.3; P=0.04). Post hoc analysis of the mean scores over the trial revealed estimated treatment effects for talc of −5.7 points (95% CI, −9.8 to −1.6) for chest pain (P=0.007) and −3.6 points (95% CI, −8.5 to 1.3) for dyspnea (P=0.15).

Effusion Complexity and Size
No significant between-group difference was seen in effusion size, as assessed by thoracic ultrasonography, during the trial. In addition, no significant difference was observed in the degree of septation at any time point during the trial.

Mortality and Adverse Events
During the trial, 21 patients died (7 in the talc group and 14 in the placebo group). None of the deaths were attributed to the trial interventions. The odds ratio for death was 0.45 (95% CI, 0.17 to 1.24) favoring the talc group, but this result was not significant (P=0.13).

No significant difference between the talc group and the placebo group was seen in the number of participants who had adverse events (odds ratio, 0.90; 95% CI, 0.47 to 1.71; P=0.74), with 68% of the events (84 of 123 events) being considered to be unrelated to the trial after blinded independent review. The most common reported events were due to underlying disease progression or distant fluid accumulation. Blockage of the indwelling pleural catheter occurred
in 3 of 76 patients (4%) in the placebo group and in 5 of 78 (6%) in the talc group (Table 2, and Tables S19 and S20 in the Supplementary Appendix).

**DISCUSSION**

Our randomized trial compared the combination of talc and indwelling pleural catheter with placebo and indwelling pleural catheter in patients with malignant pleural effusion who were outpatients. Our primary-outcome results, which were backed up by robust sensitivity analyses, strongly suggest that the administration of talc through an indwelling pleural catheter was significantly more efficacious than the use of an indwelling pleural catheter alone among patients without substantial lung entrapment. Patients in the talc group were more than twice as likely as those in the placebo group to meet the criteria for successful pleurodesis. Success rates at day 70 suggested that pleurodesis was maintained to a point that is clinically relevant for patients with short median survival.7

Although the use of an indwelling pleural catheter has been shown to lead to a reduction in symptoms,20 there are potential drawbacks to long-term treatment, including the inconvenience of regular drainage (with associated health care costs)21 and risks of infection.22 Previous data suggest an average incidence of spontaneous pleurodesis of approximately 45% (at approximately 2 months) when only an indwelling pleural catheter is used.20 However, Wahidi et al. recently examined the influence of frequency of drainage through an indwelling pleural catheter (daily vs. standard alternate day) in a population of patients with malignant pleural effusion in North
America, and they found rates of successful pleurodesis at 12 weeks of 47% in the daily-drainage group versus 24% in the standard-drainage group. In addition, the rate of device removal in the indwelling-pleural-catheter group in the Australasian Malignant Pleural Effusion (AMPLE) trial was 28.8%. In combination with the results of our trial, these data imply that the true incidence of spontaneous pleurodesis is considerably lower than the incidence that has been previously reported in retrospective case series.

Approximately 40% of the patients who had undergone randomization had at least one adverse event during the trial — an overall proportion similar to that in the indwelling-pleural-catheter group of the Second Therapeutic Intervention in Malignant Effusion (TIME2) trial. However, the majority (68%) of the adverse events in our trial were considered to be unrelated to the intervention and tended to represent disease progression. We did not observe any excess in adverse events — specifically, blockage of the indwelling pleural catheter, fluid complexity, drainage complications, or death — in the talc group. This finding suggests that the administration of talc through an indwelling pleural catheter in an outpatient setting was not detrimental, either to the patient or the device. There are limitations to our trial. During the short but intense follow-up period, we assessed the early effects of the trial intervention, but we are unable to comment on the effects of the administration of talc through an indwelling pleural catheter beyond 70 days. In addition, it could be argued that our definition of pleurodesis, although pragmatic and easily reproducible, did not attempt to assess the true degree of visceroparietal adhesion formally — for example, with the use of thoracic ultrasonography, an approach that although reported is not yet validated. Finally, because relatively high numbers of patients were excluded before randomization, the results we observed may apply to only a selected group of patients with malignant pleural effusion.

In conclusion, our data showed that patients who had malignant pleural effusion without substantial lung entrapment and who chose treatment with an indwelling pleural catheter had a greater chance of pleurodesis when talc administration was part of the treatment protocol than when the indwelling pleural catheter was used alone.

Supported by an unrestricted research grant from Becton Dickinson.

Dr. Bishop reports receiving educational fees and donated medical equipment from Rocket Medical U.K. and educational fees and equipment from Becton Dickinson; Dr. Ahmed, receiving grant support from Becton Dickinson and GE Medical; Dr. Psallidas, being employed by AstraZeneca in addition to his affiliation with University of Oxford; Dr. Lee, receiving grant support and medical supplies from Rocket Medical U.K. and fees for serving on an advisory board from Becton Dickinson; Dr. Rahman, receiving consulting fees from Rocket Medical U.K.; Dr. Miller, receiving lecture fees and travel support from Gilead Sciences and lecture fees from Janssen, Merck, and ViV Health; and Dr. Maskell, receiving grant support and consulting fees from Becton Dickinson and grant support from Rocket Medical U.K. No other potential conflict of interest relevant to this article was reported.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

We thank Ms. Sharon Stander, Ms. Bethan Watts, Mr. David Hutton, Dr. Ramon Luengo-Fernandez, Ms. Karen Cooper, Dr. Ly-Mee Yu, Dr. Tim Peto, Dr. Duncan Geddes, Dr. Amelia Clive, Dr. Oliver Bintcliffe, Dr. Duneshe de Fonseka, Dr. Anthony Eedy, Ms. Penny Senior, Ms. Janet Iles, Mr. Simon Strange, and all the members of the research teams at each site, the community nursing teams, and the patients and carers for contributions to the conduct of the trial.

APPENDIX


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Healthcare NHS Foundation Trust, North Shields (D.C.), Sherwood Forest Hospitals NHS Foundation Trust, Sutton-in-Ashfield (M.R.), NHS Ayrshire and Arran, Ayr (A.G.), Worcester Acute Hospitals NHS Trust, Worcester (C.H.), Royal United Hospitals Bath NHS Foundation Trust, Bath (J.W.), Blackpool Teaching Hospitals NHS Foundation Trust, Blackpool (T.S.S.), Aintree University Hospitals NHS Foundation Trust, Liverpool (B.C.), Hampshire Hospitals NHS Foundation Trust, Winchester (S.G.), and the Oxford Respiratory Trials Unit, University of Oxford (I.P., N.M.R.), the Oxford University Hospitals NHS Foundation Trust (I.P., N.M.R.), and the Oxford NIHR, Biomedical Research Centre (N.M.R.), Oxford — all in the United Kingdom; and the Institute for Respiratory Health, University of Western Australia, and Sir Charles Gairdner Hospital, Perth, WA, Australia (I.C.G.L.).

REFERENCES


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