The influence of meteorological variables on the development of deep venous thrombosis

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Summary
The influence of weather on deep venous thrombosis (DVT) incidence remains controversial. We aimed to characterize the temporal association between DVT and meteorological variables including atmospheric pressure. Data relating to hospital admissions with DVT in Scotland were collected retrospectively for a 20 year period for which corresponding meteorological recordings were available. Weather variables were calculated as weighted daily averages to adjust for variations in population density. Seasonal variation in DVT and short-term effects of weather variables on the relative risk of developing DVT were assessed using Poisson regression modelling. The models allowed for the identification of lag periods between variation in the weather and DVT presentation. A total of 37,336 cases of DVT were recorded. There was significant seasonal variation in DVT with a winter peak. Seasonal variation in wind speed and temperature were significantly associated with seasonal variation in DVT. When studying more immediate meteorological influences, low atmospheric pressure, high wind speed and high rainfall were significantly associated with an increased risk of DVT approximately 9–10 days later. The effect was most strikingly demonstrated for atmospheric pressure, every 10 millibar decrease in pressure being associated with a 2.1% increase in relative risk of DVT. Alterations in weather have a small but significant impact upon the incidence of DVT. DVT is particularly associated with reduction in atmospheric pressure giving weight to the hypothesis that reduced cabin pressure in long haul flights contributes to DVT. These findings have implications for our understanding of the pathogenesis of DVT.

Keywords
Deep venous thrombosis, venous thromboembolism, weather, atmospheric pressure, epidemiology

Introduction
In the US venous thromboembolism (VTE) has an estimated incidence exceeding 1 per 1000 of the population, contributing to over 50,000 deaths per annum (1). While a number of well-defined risk factors for the development of VTE are recognised (such as immobility, recent surgery, recent fracture, pregnancy, malignancy and oestrogen therapy) the influence of meteorological variables remains controversial. Pulmonary embolism (PE) has been associated with low atmospheric pressure, low temperature, high rainfall, high relative humidity and high vapour pressure (2–6). The effects of meteorological variables on deep venous thrombosis (DVT) are less well characterised. Overall, the emergence of a consistent effect of weather on VTE has been hampered by the requirement for large datasets to detect relatively small influences on the risk of VTE, and a tendency for previous, smaller studies to yield conflicting conclusions.

Scotland is a comparatively small country both geographically and demographically (population approximately 5.1 million), with a relatively stable population, well-established meteorological records and a centralised diagnostic coding system for hospital admissions. This combination presented us with the opportunity to make a detailed assessment of the associations between DVT and variations in weather. The aim of this study was therefore to investigate the temporal association between DVT and meteorological variables, with particular emphasis on atmospheric pressure.
Methods

Data on all discharges from Scottish hospitals, covering the country’s entire population, are compiled at the Information Services Division (ISD), National Health Service (NHS) Scotland. Diagnoses are recorded on each patient’s hospital discharge summary using standard International Classification of Disease (ICD) codes. All acute presentations to hospital with a diagnosis of DVT over the period 1st January 1981 to 31st May 2001 were included in the study. Patients were considered to have had DVT if the principal diagnosis recorded was ICD9 (4511 or 4151) or ICD10 (I80). The index date for each patient was taken to be the date of admission to hospital.

Data from weather stations in each of the fifteen NHS Trusts in Scotland were recorded each day during the corresponding period and provided by the National Meteorological Office. Measured variables included atmospheric pressure, temperature (minimum and maximum), hours of sunshine, rainfall, snowfall and wind speed. Atmospheric pressure and wind speed were calculated as the average of four 6-hourly readings taken each day. Average daily weather statistics for the whole of Scotland were calculated as weighted daily averages of the values recorded at the 15 weather stations, with weights taken as the population sizes of the NHS Trusts. This ensured that weather statistics most closely matched the population covered.

To test for seasonal variation in the rate of DVT, the number of DVTs per calendar month was calculated, and a Poisson regression model was used to determine whether the months differed significantly.

On the assumption that weather may affect the incidence of DVTs through seasonal effects and/or short-term changes, models were constructed to incorporate these influences. To assess the seasonal influence, average weather statistics and numbers of DVTs were calculated for each week of the year (e.g. 1, 2, 3, …, 52) and Spearman rank correlation coefficients calculated to assess the correlations between them. To assess the short-term effects of weather, daily meteorological statistics and numbers of DVTs were analysed using Poisson regression models. These models adjusted for day of the week, seasonal trend (by fitting week of the year), time trend (to allow for the increasing incidence of DVT observed throughout the study period) and change in diagnosis rates following the switch from ICD9 to ICD10 coding in April 1997. On the assumption that there would be a delay between any biological influence of meteorological variables and clinical presentation with DVT, models included lag periods for the effect of weather varying from 0 to 21 days prior to presentation.
Results

A total of 37,336 cases of DVT were recorded in the study period. The mean age of the patients was 60.8 (SD 17.6) years and 48.0% were male. There was a significant seasonal variation in the incidence of DVT, with the highest average incidence in January and the lowest in August (p<0.0001; Figure 1). Meteorological data for the study period are described in Table 1 and all measured weather variables had a highly significant seasonal variation (p<0.0001). The seasonal variation in DVT was significantly associated with the seasonal variation in wind speed (p=0.006), minimum and maximum temperature (p=0.0009 and 0.001 respectively), and snowfall (p=0.01), but not with atmospheric pressure, rainfall or hours of sunshine.

When considering short-term influences of weather, low atmospheric pressure, high wind speed and high rainfall were associated with significantly increased rates of DVT (Table 2). The association was most striking for atmospheric pressure (Figure 2). For each variable the association was characterised by a lag period, typically of the order of 9–10 days. The data suggest that a relative decrease in atmospheric pressure results in an increased risk of presenting DVT some 6 to 12 days later. The risk was greatest for a lag period of 9 days with the relative rate of DVT increased by 2.06% (95% CI 1.14–2.99%) per 10 millibars decrease in pressure. Similarly an increased wind speed was associated with a significantly increased rate of presenting DVT 9 to 12 days later, the greatest increase being identified for a lag period of 10 days. An increase in rainfall is associated with a significantly increased rate of presenting DVT 2, 10, 11 and 13 days later, the relative rate being greatest for a lag period of 10 days. High snowfall on the date of admission was associated with a reduction in the rate of presenting with DVT. No clear association was found between the incidence of DVT and the short term effect of temperature or hours of sunshine.

Discussion

The study benefits from the large number of patients accumulated using a consistent national system for recording health outcome data throughout Scotland over a 20 year period. As a small country (approximately 79,000 km²) with a temperate climate influenced largely by the Atlantic Gulf Stream, widely ranging extremes of weather in different locations on the same day are relatively unlikely.

It is recognised by physicians and radiologists involved in the diagnosis and management of venous thromboembolism that, although a common disease, the numbers of patients presenting with the disease varies greatly from week to week and month to month. Our findings suggest that meteorological factors may contribute to this variability. They describe a seasonal variation in the incidence of DVT, with winter predominance. They also suggest that low atmospheric pressure, high rainfall and high wind speed are associated with a small but significantly increased rate of DVT with a distinct lag period (typically 9–12 days) characterising the relationship between these variables and subsequent presentation with DVT. Small calf DVT are often initially asymptomatic and it is recognised that there is often a lag time between the initial insult where DVT first develops and the

Table 1: Mean daily values for measured meteorological variables by calendar month.

<table>
<thead>
<tr>
<th></th>
<th>Jan</th>
<th>Feb</th>
<th>Mar</th>
<th>Apr</th>
<th>May</th>
<th>Jun</th>
<th>Jul</th>
<th>Aug</th>
<th>Sep</th>
<th>Oct</th>
<th>Nov</th>
<th>Dec</th>
<th>Ave. within month SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure (millibars)</td>
<td>1009.7</td>
<td>1011.7</td>
<td>1009.9</td>
<td>1012.7</td>
<td>1015.2</td>
<td>1014.8</td>
<td>1014.3</td>
<td>1013.3</td>
<td>1011.6</td>
<td>1008.9</td>
<td>1009.3</td>
<td>1008.6</td>
<td>0.5</td>
</tr>
<tr>
<td>Wind speed (knots)</td>
<td>9.55</td>
<td>9.91</td>
<td>9.72</td>
<td>8.29</td>
<td>7.66</td>
<td>7.37</td>
<td>7.07</td>
<td>7.04</td>
<td>7.65</td>
<td>8.28</td>
<td>8.17</td>
<td>8.46</td>
<td>0.14</td>
</tr>
<tr>
<td>Minimum temperature (°C)</td>
<td>0.82</td>
<td>0.97</td>
<td>1.83</td>
<td>2.98</td>
<td>5.18</td>
<td>7.70</td>
<td>9.68</td>
<td>9.60</td>
<td>7.91</td>
<td>5.37</td>
<td>2.96</td>
<td>1.28</td>
<td>0.09</td>
</tr>
<tr>
<td>Maximum temperature (°C)</td>
<td>5.94</td>
<td>6.35</td>
<td>7.91</td>
<td>10.02</td>
<td>13.07</td>
<td>14.95</td>
<td>16.94</td>
<td>16.80</td>
<td>14.48</td>
<td>11.33</td>
<td>8.37</td>
<td>6.50</td>
<td>0.09</td>
</tr>
<tr>
<td>Rainfall (mm)</td>
<td>3.35</td>
<td>2.89</td>
<td>2.87</td>
<td>1.92</td>
<td>1.78</td>
<td>2.01</td>
<td>2.03</td>
<td>2.31</td>
<td>3.18</td>
<td>3.61</td>
<td>3.36</td>
<td>3.49</td>
<td>0.13</td>
</tr>
<tr>
<td>Daily sunshine (hours)</td>
<td>1.39</td>
<td>2.39</td>
<td>3.23</td>
<td>4.54</td>
<td>6.00</td>
<td>5.39</td>
<td>5.12</td>
<td>4.86</td>
<td>3.91</td>
<td>2.80</td>
<td>1.85</td>
<td>1.09</td>
<td>0.10</td>
</tr>
<tr>
<td>Snow (probability)</td>
<td>0.196</td>
<td>0.160</td>
<td>0.088</td>
<td>0.017</td>
<td>0.004</td>
<td>0.002</td>
<td>0.004</td>
<td>0.003</td>
<td>0.002</td>
<td>0.001</td>
<td>0.037</td>
<td>0.124</td>
<td>0.004</td>
</tr>
</tbody>
</table>
time of clinical presentation and diagnosis at hospital. The finding of a significant correlation between a drop in atmospheric pressure and presentation with DVT puts that delay at maximum between days 6 and 12. High rainfall 2 days prior to presentation was also statistically significant in predicting DVT, however the biological significance is unclear as high rainfall for lag periods of 1 and 3 days was not significant.

Various studies have addressed the question of seasonal variation in VTE. A large retrospective study involving 65,000 cases of DVT and over 60,000 cases of PE in France found clear evidence for seasonal variation (7), broadly in keeping with smaller studies from Europe and Australia (3, 8–12). This effect appears to extend beyond idiopathic DVT, having also been described for post-operative DVT (13). Importantly, in studies reporting a seasonal variation the trend for a winter and autumn predominance has been relatively consistent. It must be emphasised that seasonal variation has not been observed by all investigators (14–17), however it may be relevant that the two largest studies to date (our own study and that by Boulay et al, 7) found a trend towards winter predominance.

Many biological variables could potentially contribute to the seasonal influence on VTE. For example a procoagulant profile is known to develop in venous blood during colder months (18). In addition respiratory infections are more common in winter

Table 2: Short-term effects of weather on incidence of DVTs, adjusted for seasonality. Results are expressed as percentage relative rate.

<table>
<thead>
<tr>
<th>Days prior to admission</th>
<th>Atmospheric Pressure (per 10 millibar decrease)</th>
<th>Windspeed (per 1 knot decrease)</th>
<th>Daily rainfall (per mm increase)</th>
<th>Snow (if any)</th>
<th>Maximum Temp (per 1°C decrease)</th>
<th>Minimum Temp (per 1°C decrease)</th>
<th>Daily sunshine (per hour decrease)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.19</td>
<td>0.28</td>
<td>0.10</td>
<td>–13.04*</td>
<td>–0.45</td>
<td>–0.53</td>
<td>0.35</td>
</tr>
<tr>
<td>1</td>
<td>0.54</td>
<td>0.32</td>
<td>–0.13</td>
<td>–8.86</td>
<td>–0.29</td>
<td>0.03</td>
<td>0.16</td>
</tr>
<tr>
<td>2</td>
<td>0.19</td>
<td>–0.05</td>
<td>0.56*</td>
<td>–1.14</td>
<td>–0.09</td>
<td>0.34</td>
<td>0.33</td>
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<tr>
<td>3</td>
<td>0.33</td>
<td>0.20</td>
<td>0.18</td>
<td>3.16</td>
<td>0.41</td>
<td>0.21</td>
<td>–0.24</td>
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<tr>
<td>4</td>
<td>0.85</td>
<td>0.26</td>
<td>–0.12</td>
<td>–1.23</td>
<td>0.34</td>
<td>0.23</td>
<td>0.16</td>
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<tr>
<td>5</td>
<td>1.18</td>
<td>0.22</td>
<td>0.15</td>
<td>–3.04</td>
<td>0.36</td>
<td>0.42</td>
<td>0.15</td>
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<tr>
<td>6</td>
<td>1.30*</td>
<td>0.24</td>
<td>0.36</td>
<td>–3.34</td>
<td>0.53</td>
<td>0.25</td>
<td>0.13</td>
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<tr>
<td>7</td>
<td>1.46*</td>
<td>0.31</td>
<td>0.27</td>
<td>–4.85</td>
<td>0.67</td>
<td>0.60</td>
<td>0.44</td>
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<tr>
<td>8</td>
<td>1.82*</td>
<td>0.20</td>
<td>0.40</td>
<td>–3.23</td>
<td>0.48</td>
<td>0.38</td>
<td>0.25</td>
</tr>
<tr>
<td>9</td>
<td>2.06*</td>
<td>0.52*</td>
<td>0.30</td>
<td>–1.76</td>
<td>0.51</td>
<td>0.17</td>
<td>0.26</td>
</tr>
<tr>
<td>10</td>
<td>1.85*</td>
<td>0.59*</td>
<td>0.80*</td>
<td>–2.45</td>
<td>0.24</td>
<td>–0.04</td>
<td>0.30</td>
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<tr>
<td>11</td>
<td>1.27*</td>
<td>0.49*</td>
<td>0.59*</td>
<td>–1.26</td>
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<td>0.18</td>
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<tr>
<td>12</td>
<td>1.26*</td>
<td>0.54*</td>
<td>0.29</td>
<td>–2.39</td>
<td>0.01</td>
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<td>13</td>
<td>0.94</td>
<td>0.34</td>
<td>0.46*</td>
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<td>14</td>
<td>0.93</td>
<td>0.32</td>
<td>0.15</td>
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<td>–0.06</td>
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<td>15</td>
<td>1.01</td>
<td>0.25</td>
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<td>–2.19</td>
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<td>16</td>
<td>0.61</td>
<td>0.09</td>
<td>0.19</td>
<td>–0.09</td>
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<td>0.08</td>
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<td>17</td>
<td>0.76</td>
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<td>18</td>
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<td>21</td>
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<td>0.17</td>
<td>0.36</td>
<td>–3.30</td>
<td>–0.36</td>
<td>–0.40</td>
<td>0.40</td>
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</table>
months and are themselves associated with an increase in VTE (19). Furthermore, it may be plausible to argue that populations are more sedentary during the winter.

Our finding that low atmospheric pressure is associated with DVT is broadly in keeping with previous observations in VTE. In particular Esquenet et al. (20) found an association between DVT and low atmospheric pressure which was more pronounced as pressure gradients widened. In an earlier study Scott et al. (4) found that PE was associated with a decrease in atmospheric pressure. Importantly, they also found a lag effect but this was of the order of 3 days as opposed to the longer interval described here. A Turkish study found that PE was more common in spring, which in turn was associated with relatively low atmospheric pressure (6).

In contrast, studies by Becker et al. (2) and Clauss et al. (5) failed to demonstrate an association between atmospheric pressure (or temperature) and PE. Interestingly however these studies, both of which were smaller than the present study, identified a relationship between PE and high rainfall in keeping with our own observations.

The emerging picture for VTE finds some parallels in studies of arterial thrombosis (21). For example myocardial infarction has variously been associated with increased incidence in the winter months, low temperature, and low/falling atmospheric pressure (22–24).

Our analyses of short term weather effects (Table 2) were adjusted for seasonality and therefore the association found between meteorological variables and DVT is not an epiphenomenon based on seasonality. This in turn begs the question of how influential atmospheric pressure, rainfall and wind speed are in the development of DVT. Our data suggest that the influence is small but statistically significant. To place this in context a relative decrease in atmospheric pressure of 10 millibars predicts for a 2% increase in the rate of DVT nine days later (Table 2). The mean daily variation (SD) in atmospheric pressure in Scotland during the study period was 12.8 millibars. Thus on average pressure is predicted to cause DVT incidence to rise or fall by 2.6% each day. Similarly, for every increase in rainfall of 1 mm or for every 1 knot increase in wind speed, the rate of DVT 10 days later was increased 0.8% and 0.6% respectively, while mean daily variability (SD) in rainfall and wind speed in Scotland were 3.4 mm and 3.8 knots respectively.

Weather statistics are inter-related, for example low pressure often accompanies a period of heavy rainfall. Therefore the effects of pressure, wind speed and rainfall on the incidence of DVTs cannot be considered additive. Although statistical models can demonstrate which of the measurements is the most predictive statistically, they cannot provide evidence for a causal relationship to DVT. However it is tempting to speculate on biological plausibility linking these factors to DVT. In this regard it has
been shown that hypobaric hypoxia, but not normobaric hypoxia, is associated with hypercoagulability in humans (25–27), while hypobaric conditions favour DVT formation in postoperative rabbits (28). Toff et al. (29) did not show a statistical increase in hypercoagulability in relation to hypobaric oxygen in a group of patients without known thrombophilia. However their exploratory analysis did show greater dispersion with more outliers in the distribution of changes in coagulation activation in the hyperbaric than in the normobaric limbs of their study. They accepted that some individuals may respond differently and were unable to say whether this finding was due to chance or to a genuine biological difference. Our hypothesis is that some, but not all, individuals are susceptible to the effects of reduced pressure and that those who are susceptible are more likely to be those with a pre-existing thrombotic tendency. In the background, a vigorous debate continues to surround the effect of flying on VTE (30–35).

The cabins of commercial aircraft are generally pressurised to a level equivalent to 8000 feet above sea level (700 millibars), and have relatively low humidity. Evidence for a small increase in the rate of DVT on particularly long flights seems to be emerging and it could be speculated that our data broadly support reduced air pressure as a plausible contributing factor towards the development of DVT in long haul flights in susceptible individuals.

The effects of rainfall and wind speed on DVT have not received much scientific attention. It has been postulated that prothrombotic pollutants could be carried as condensation nuclei in water droplets (5). This contention could be extended to encompass increased dispersal of atmospheric pollutants and/or organic/infective particles by increased wind speeds. However this remains entirely conjectural and has not been scientifically tested. Alternatively the relationship with rainfall and wind speed may have arisen purely as a consequence of their association with atmospheric pressure.

Several potential limitations of this study should be acknowledged, particularly the retrospective design. This raises concerns especially over accuracy of diagnosis of DVT, and the potential for missed cases. Available evidence suggests that over the duration of the study hospital-based diagnosis of DVT in Scotland was increasingly based on objective investigations rather than clinical assessment alone (36, 37) and diagnostic confirmation is therefore likely to have been high. It is also reassuring that the incidence of DVT over the 20 year study period (approximately 30 per 100,000 per annum) is broadly in line with other incidence estimations (1). However, any inconsistencies in diagnosis are unlikely to alter the seasonal and short term associations demonstrated. Also, multiple tests of significance have been carried out to assess the different weather statistics and lag periods and caution is needed when interpreting significance levels. However, the overall pattern of results across the lag periods helps to confirm the presence of a genuine effect (38). For example, the effect of atmospheric pressure is negligible on the day of presentation, significant during days 6–12 reaching a peak at 9 days and then negligible again by 21 days.

In summary low atmospheric pressure, high rainfall and high wind speed are associated with a small but significant increase in the rate of DVT. The mechanisms and interactions involved deserve further scientific attention.

References

What is known about this topic?
- Several, but not all, previous studies have shown a predominance of DVT in winter.
- It has been postulated that changes in atmospheric pressure may contribute towards DVT development.
- Some but not all previous studies have demonstrated that a drop in atmospheric pressure is associated with an increased incidence of venous thromboembolism.

What does this paper add?
- In a large cohort of patients this paper has shown that low atmospheric pressure, high rainfall and high wind speed are associated with a small but significant increase in the rate of DVT.
- The findings have been adjusted for seasonality confirming that the association found between meteorological variables and DVT is not an epiphenomenon based on seasonality.
- The strongest association is with a reduction in atmospheric pressure with a relative decrease in atmospheric pressure of 10 millibars predicting for a 2% increase in the rate of DVT nine days later.