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## Updated and Expanded Study of Polycythemia Vera and Other Myeloproliferative Neoplasms in the Tri-County Area

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### Abstract

**Introduction**—The results of a 2001–2005 polycythemia vera (PV) investigation in Eastern Pennsylvania revealed a disease cluster plus underreporting and false reporting to the Pennsylvania Cancer Registry (PCR).

**Purpose**—The objectives of this study were 1) to assess PV reporting to the PCR in 2006–2009, 2) to determine whether a cancer cluster persisted, and 3) to determine whether other myeloproliferative neoplasms (MPNs), including essential thrombocytopenia (ET), were subject to similar reporting problems.

**Methods**—Cases were identified from: 1) PCR records from the Tri-County, 2) reviewing billing records at Tri-County hematologist/oncologist offices, and 3) self-identification. An expert panel of physicians reviewed medical records and determined “true,” “false,” or “indeterminate” cases reported to the PCR. The analyses were conducted to determine sensitivity and positive predictive value (PPV) of case reporting to the PCR, estimate cancer incidence rates, and evaluate the presence of cancer clusters.

**Results**—Of 290 cases identified, 90% were from the original PCR, 9% from billing records, and 1% from self-report. Fifty-five cases consented to participate, and medical records were obtained for 44. The expert panel determined that 45% were true cases, 32% were false cases, and 23% were indeterminate. PV had 100% (95% CI, 59–100) sensitivity, but only 47% PPV (95% CI, 20–70); ET had 78% (95% CI, 47–99) sensitivity and 100% PPV (95% CI, 59–100). Low participation and chart review rates led to rates with wide confidence intervals. We did not identify any PV cancer clusters, but we did identify a cluster of 9 ET cases in the Wilkes-Barre, Pennsylvania area.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official views or positions of the Centers for Disease Control and Prevention/Agency for Toxic Substances and Disease Registry or the Department of Health and Human Services.

**Conclusion**—The current study was limited by the low response rate (22%) from MPN patients in the Tri-County area. This study identified 47% PPV for PV reporting and 100% PPV for ET.

### Keywords

epidemiologic methods; epidemiology; incidence; myeloproliferative disorders; polycythemia vera; registries

## Background

Polycythemia vera (PV), a chronic hematologic malignancy involving an overproduction of red blood cells, belongs to a class of neoplasms classified by the World Health Organization (WHO) as myeloproliferative neoplasms (MPNs). All of the MPNs are hematopoietic stem cell disorders of common clonal heritage, characterized by bone marrow proliferation and peripheral blood erythrocytosis, thrombocytosis, or granulocytoses.<sup>1</sup> In addition to PV, the MPNs include chronic myeloid leukemia (CML), essential thrombocytopenia (ET), primary myeloid fibrosis (PMF), and other related and unclassifiable MPNs, such as chronic neutrophilic leukemia.<sup>1</sup> In 2005, a somatic point mutation in the *JAK2* gene of hematopoietic cells was discovered; this mutation, *JAK2V617F*, is found in more than 90% of persons with PV and in approximately 50% of persons with ET and PMF.<sup>2</sup> Factors leading to this acquired genetic mutation are unknown.

In 2004, physicians and residents in the Tamaqua area of eastern Pennsylvania became concerned about the diagnosis of PV in 4 persons living on the same street with nearby toxic waste sites.<sup>3</sup> In 2005, the Pennsylvania Department of Health (PADOH) determined a higher incidence of PV in Luzerne and Schuylkill counties. Upon request from PADOH, the Agency for Toxic Substances and Disease Registry (ATSDR) assessed sensitivity and positive predictive value (PPV) of PV reporting to the Pennsylvania Cancer Registry (PCR) for Luzerne, Schuylkill, and Carbon counties. ATSDR used findings to estimate PV incidence rates from 2001 (when MPNs first became reportable) through 2005 in these 3 counties. The results of this evaluation indicated that inaccurate reporting of PV to the PCR led to PV risk estimates that were inflated over true values by 13% to 62%.<sup>2</sup> The ATSDR study did identify a statistically significant cluster of PV cases near the intersection of the 3 counties. The incidence of PV in this cluster area was more than 4 times that of the entire Tri-County area.<sup>3</sup> Several hazardous waste exposure sites were identified near the cluster area.<sup>3</sup> In 2009, Congress funded ATSDR to continue this investigation. ATSDR is overseeing 18 projects related to this cluster with partners including the PADOH, the Pennsylvania Department of Environmental Protection, and various universities and private organizations<sup>4</sup>.

The MPNs represent an inter-related series of diseases that may have a common origin, and the entire spectrum of these diseases has not yet been evaluated in the Tri-County area. The current study was designed as an update and expansion of the original ATSDR study to determine if 1) sensitivity and PPV of PV reporting had improved in 2006–2009, 2) reporting of PMF, ET and related MPNs was complete and accurate in the Tri-County area for 2001–2009, and 3) rates of these related MPNs were elevated in the Tri-County area. The CML results are reported separately<sup>5</sup>.

## Methods

### Case Ascertainment

The first phase of case ascertainment consisted of obtaining information on all cases reported to the PCR with residence at time of diagnosis in Carbon (FIPS [Federal Information Processing Standards] code 42025), Luzerne (FIPS code 42079), or Schuylkill (FIPS code 42107) County and the following dates of diagnosis and histology codes: 2006–2009 for PV (histology code 9950); 2001–2009 for ET (histology code 9962), PMF (histology code 9961), and MPN not otherwise specified (MPN/NOS) (histology code 9960). Cases of acute panmyelosis with myelofibrosis (APMF) (histology code 9931) were also reviewed to determine whether PMF cases had been misclassified.

In the second phase of case identification (enhanced casefinding), PCR staff conducted active casefinding outreach by visiting all 9 hematologist/oncologist offices within the Tri-County area and 2 in surrounding counties to ascertain cases that should have been reported to the PCR but were not in the PCR files. The PCR staff reviewed patient billing records from each office. PCR staff reviewed the medical records of patients with MPN-associated billing codes who were not already included in the PCR files, and abstracted and reported those eligible cases to study investigators. Persons with MPNs could also self-identify to study investigators and were informed about the study by press releases about the study, and had multiple opportunities to meet with investigators in person during visits to the Tri-County area.

### Data Collection

Potential cases were asked to participate in 3 phases of data collection: release of medical records related to their MPN diagnosis, a telephone survey, and a JAK2 mutation test (if one had not already been performed). Potential cases were mailed letters of introduction, consent forms, and releases for medical records (for review by the expert panel), and asked to return signed forms indicating their participation.

The study coordinator requested copies of outpatient and inpatient medical records relevant to the MPN diagnosis. The medical records submitted were reviewed. Incomplete medical record requests were also identified. The study coordinator telephoned the offices of medical providers and asked about the availability of medical records that appeared to be missing; multiple phone calls and repeated attempts to obtain records from noncompliant offices were made.

Patients not previously tested were asked to consent to JAK2 mutation testing. If they agreed, an appointment was scheduled at a local hospital for testing. A 10-cc blood sample was collected in an ethylenediaminetetraacetic acid (EDTA) blood collection tube and sent to the Division of Molecular Diagnostics, Department of Pathology, University of Pittsburgh Medical Center, for detection of the JAK2 mutation by allele-specific polymerase chain reaction.

## Expert Panel Review

The 5-member expert panel consisted of 4 board-certified hematologist/oncologists and 1 family practitioner. The study investigators assembled records received from medical providers and placed them in chronological order. Three expert panel members independently reviewed each case's medical records. Expert panel members were instructed to review cases in 2 ways: 1) by applying conventional hematology practice standards at the time of diagnosis to determine the appropriateness or suitability of the diagnosis and 2) by classifying cases according to the 2008 WHO guidelines. Separate classification forms were developed for each disease. Expert panel members gave a determination for each case as "definitely" or "probably" a case (true cases), "possibly" a case (indeterminate), "definitely not" or "probably not" a case (false cases). At least 2 of the 3 opinions needed to be in agreement for true and false cases; if the members had different opinions or at least 2 members were not in agreement, the case was classified as indeterminate.

## Data Analysis

After cases were categorized as "true," "indeterminate," or "false," we determined the sensitivity and PPV of the PCR. Sensitivity was calculated as the number of cases originally reported to the PCR divided by the total number of all true cases which includes those originally reported plus those found by reviewing billing records and self-report. PPV was calculated as the number of true cases originally reported to the PCR divided by the total number of cases, which included false positives, originally reported to the PCR. To adjust the PCR-reported incidence rates for sensitivity and PPV, we divided the Tri-County area incidence rate by the sensitivity then multiplied by the PPV. The 95% confidence intervals were calculated using the exact method.<sup>9</sup>

To identify geographic subregions with an elevated incidence of an MPN, we included true cases and ZIP code- and census tract-level population counts from the US 2000 Census<sup>6</sup> with ZIP code or census tract centroids (calculated from US Census Bureau<sup>7</sup> shape files using ArcGIS Version 9 tools). We used SaTScan (Version 7.0.3),<sup>8</sup> designed to analyze spatial, temporal, and space-time data using the corresponding scan statistics, and we used the Poisson-based model for spatial data, as well as the space-time permutation model. The discrete Poisson-based model considers the number of events in a geographical location as Poisson-distributed, based on the underlying population at risk. Under the null hypothesis, the expected number of cases in each area is proportional to its population size, or person years. The analysis is then conditioned on the total number of cases observed. The space-time permutation model uses only case data and scans for unusual occurrences in space and time simultaneously. ATSDR previously used the Poisson-based model for spatial data to identify a statistically significant primary geographic cluster of PV cases diagnosed in 2001–2005 in a region with a history of environmental contamination.<sup>3</sup> This study was approved by the Institutional Review Boards of the University of Pittsburgh and the Pennsylvania Department of Health.

## Results

### Case Ascertainment

We identified a total of 290 potential MPN cases from the original PCR reports (n = 260), the enhanced casefinding (n = 25), and self-identification (n = 5). Overall, the original PCR data contributed approximately 90% of identified cases, with 42% reported as PV (Table 1). The PCR casefinding efforts identified an additional 25 cases, of which 56% (n = 14) were ET. Five cases self-identified to investigators: 4 PV cases and 1 ET case.

### Case Participation

As shown in Figure 1, we determined a mailing address for 253, or 87%, of 290 cases. Of these, 58 consented (22%), 53 refused (21%), 2 (1%) were unable to consent, and 140 (55%) did not respond, despite numerous mailings and phone calls.

Over 90% of participants consenting to the study agreed to the interview (n = 54) and release of medical records (n = 55), but less than 20% consented to the blood draw (n = 10) (Figure 1). Of the 55 participants who agreed to the release of medical records, we were not able to obtain records for 11 (20%). Some physician offices (%) did not send records (n = 6) or required proof of executorship from the deceased cases' estates (n = 5).

### Expert Panel Review and Case Determination

Forty-four medical records were sent to expert panel members for review. Of these, 20 (45%) were determined to be true cases, 10 (23%) were indeterminate, and 14 (32%) were false (Figure 1). The expert panel members reached a unanimous opinion for 29 of the 44 cases reviewed (66%). PV had the lowest agreement rate (52%; 11/21 unanimous opinion) (data not shown).

### Sensitivity and PPV of PCR Reporting

Case determination status by histology is provided in Table 2. ET had the highest percentage determined to be true cases (67%), followed by MPN/not otherwise specified (NOS) (60%), and PV and PMF (33%). Of the 44 evaluated cases, 36 were originally reported to the PCR, 3 were identified by review of billing records and 5 were self-identified. Seventeen of the 20 true cases were from the PCR; 2 were from billing records (1 ET and 1 PMF); and 1 from self-identification (ET).

Additional information about the indeterminate and false judgments is provided in Table 3. The majority of the indeterminate determinations (n = 7; 70%) were due to not enough information being provided in the medical records regarding criteria used for diagnosis. Of the false cases, many were determined to have a non-MPN diagnosis, primarily secondary polycythemia in patients diagnosed with PV. One self-reported case was deemed indeterminate but was probably a secondary polycythemia case. Three self-reported cases were deemed false: 1 did not have enough information in the medical records for the experts to make a determination, 1 was determined to be a JAK2+ non-MPN, and 1 was an "other MPN" diagnosis (PMF).

Table 4 shows the estimated sensitivity and PPV of the PCR. Sensitivity of the PCR was 85% (17 true PCR cases out of 20 true cases found in the study). The PCR data file included all true cases of PV. We estimated sensitivity of PV at 100% given that we did not find any additional true PV cases by searching billing records. The only true PMF case identified was originally reported to the PCR as APMF (code 9931) and after review by the expert panel was determined to be PMF. One ET cases was identified by the additional PCR casefinding efforts and 1 self-identified, giving ET a sensitivity of 78% (7/9). PV had the lowest PPV of 47% (7/15).

### **PV and Other MPN Incidence Rates**

Shown in Table 5 are the original PCR incidence rates by histology, the study-determined sensitivity and PPV, and estimated incidence rates for comparison. As shown, our estimated ET incidence rate (2.3/100,000) is higher than the original PCR estimate (1.8/100,000). The other histologies have lower estimated incidence rates than those based on original case reporting. The estimated PV incidence rate showed the largest difference from the PCR-derived rate, at 5.3/100,000 compared to 2.5/100,000.

### **GIS Analysis**

We performed SaTScan analyses by ZIP code and census tract for the 2 histologic groups with 5 or more true cases (PV and ET). Using the 7 true PV cases, no statistically significant clusters were identified in space or in space-time (the model adjusts for any purely spatial and temporal variation) at either the ZIP code or census tract level.

Using the 9 true ET cases, we identified a statistically significant cluster at the ZIP-code level when evaluated in space ( $P < .05$ ), but not when using the space-time scan statistic ( $I = .17$ ). The cluster includes 13 ZIP codes in the Wilkes-Barre, Pennsylvania area (Figure 2). The Poisson probability of finding 9 cases in this area, where 3.05 cases were expected, is .00029 ( $P$ -value).

### **Discussion**

We found 89.5% sensitivity and 59% PPV of MPN reporting to the PCR as evaluated in this study, an expansion and update of an earlier ATSDR study in the Tri-County area of Carbon, Luzerne, and Schuylkill Counties, Pennsylvania. In this study, the expert panel review confirmed an MPN in 54% of the evaluated cases, which was slightly higher than the original ATSDR investigation. However, only 47% of the PV cases evaluated in this update were determined to be true cases compared to 53% in the original ATSDR investigation. A companion study, conducted in a demographically similar 4-county region of Pennsylvania, found 82% sensitivity and 47% PPV for PV only in 2001–2009.

These findings indicate that MPNs remain very difficult to diagnose. The 2008 WHO guidelines could improve PPV of diagnoses; however, because our study period ended in 2009, the guidelines were not widely used or applied in this study. We also found that the inaccurate reporting was due to not distinguishing PV from other conditions, namely secondary polycythemia, and a lack either of JAK2 testing or documentation of such in the medical records. These results were surprising in view of the physician and hematologist

education programs and extensive outreach that were conducted in the Tri-County area after completion of the ATSDR study,<sup>4</sup> and the current widespread availability of the JAK2 test. Among cases evaluated by the expert panel, the PPV of PV reporting was only 47%, indicating that many false cases of PV are still being reported to the PCR. However, PV sensitivity was 100%, indicating that physician education and outreach efforts regarding the importance of PV reporting may have attributed to the increased reporting of PV in the Tri-County area. ET had better PPV than PV with a higher percentage of ET cases being confirmed as true cases.

Our estimated incidence rates are lower than rates calculated from the original PCR database reflect the reporting inaccuracies. The estimated PV incidence rate was 64% lower than the original rate, 2.5 (0.8–5.10) per 100,000 instead of 5.3, after correcting for sensitivity and PPV. According to the ATSDR study results, the annual incidence of confirmed PV was between 2.4 and 3.5 per 100,000 in Carbon, Luzerne, and Schuylkill Counties in 2001–2005. The wider range of values in this study reflects the variability associated with the findings based on the low response and review rate by the expert panel.

The original ATSDR study identified a statistically significant PV cluster in the Hazleton, Pennsylvania area with an incidence rate of 3.47; they found that the remainder of the Tri-County area had an incidence rate of 0.81 and the total area had an incidence rate 1.25. We did not identify any clusters of PV by ZIP code or census tract. We found a cluster of ET cases in the Wilkes-Barre area, based on 9 cases, which was statistically significant in space, but not in the space-time model at the ZIP-code level. Given that we are evaluating a 9-year time period, we place more emphasis on the space-time results, rather than those considering space only. Two of the ET cases were diagnosed in 1 census tract in a 2-year time period. Again, while this was statistically significant, it is difficult to determine the importance of such a small number of cases. Thirteen of 99 (13%) ET cases were evaluated by the expert panel. One lived in Carbon County, 1 lived in Schuylkill County and 11 lived in Luzerne County and all 9 true cases were Luzerne County residents. When all expert panel–evaluated ET cases ( $n = 13$ ) were included in the cluster analyses, no statistically significant clusters were identified; similarly no clusters were identified using only the ET cases reported to the PCR (data not shown). The cluster identified here could be an artifact because all of the true cases resided in 1 county; ET cases in Luzerne may have been more willing to participate than cases in other counties. It may also represent a real increase of disease in Luzerne County. A more complete evaluation of ET might elucidate whether a cluster of ET persist in the Tri-County area.

This study was limited by a low incidence rate and a low response rate. The national incidence of MPNs has been estimated at 2.1 per 100,000.<sup>10</sup> Additionally, only 26% of identified cases participated, although rates were slightly higher for some diseases, including PV. We attempted to include deceased cases in this study, which was not done in the original study. The participation rate among family members of deceased cases was significantly lower than the participation rate among living cases. Another reason for the low overall participation rate may be that the Tri-County area has been subject to numerous disease investigations during the past 20 years, in part owing to the high number of environmental contaminants in the region. Not only was the original ATSDR study conducted in the Tri-

County area, but nearly a dozen other studies have been conducted in recent years<sup>3-4</sup>, including some targeting the same cases who were asked to participate in this study. The Tri-County residents may be suffering from “study fatigue” and are no longer interested in cooperating with study investigators. Although we made concerted efforts to contact and interview cases, we had few cases with complete interview data (5 PV and 6 ET cases). This was not enough information to provide any meaningful data on symptoms or past medical history.

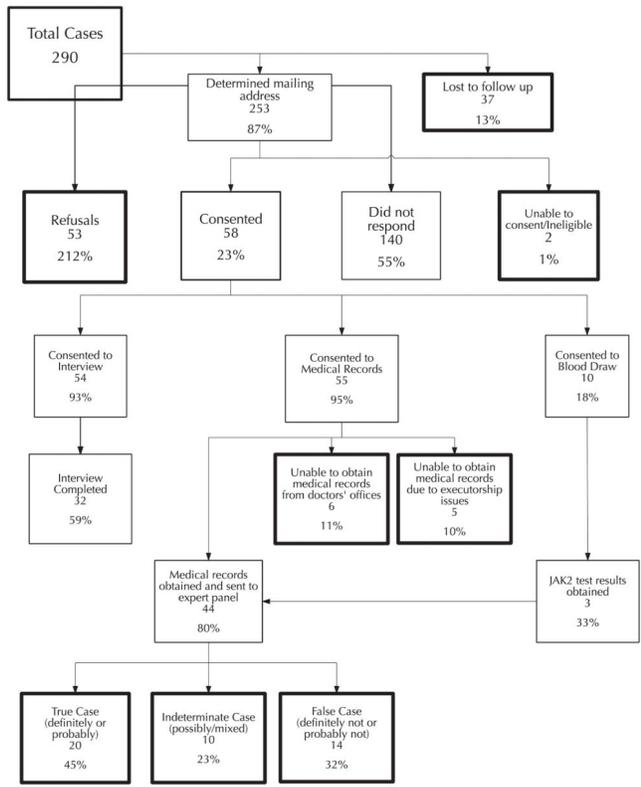
Despite the low response rate, our study provides important information on the sensitivity and PPV of MPN reporting to the PCR. We used press releases in Northeast Pennsylvania to recruit participants and performed extensive casefinding at hematology/oncology offices in and around the Tri-County area. We believe that these efforts completely and accurately captured the extent of the MPN cases in the Tri-County area for the time period of interest. Of the evaluated cases, we found that very few true MPN cases ( $n = 3$ ) were missed in the original PCR data set. The PCR’s additional casefinding efforts identified 3 true cases, indicating that the use of billing information in outpatient settings may be an effective way for the PCR to gather case information from offices not reporting MPNs. The true self-identified ET case was from a facility with a hospital registrar in the Tri-County area. Outreach efforts regarding MPN reporting should potentially be expanded to hospital registrars, and not limited to physician offices.

Our updated and expanded study of MPNs in the Tri-County area identified continued low PPV for PV reporting, but better PPV for ET. These findings suggest the need for continuing physician and registrar education on diagnostic criteria, and increased use and interpretation of JAK2 testing for MPN diagnosis. Unlike the original study, we did not find any areas with a high occurrence of PV cases, although we did identify a cluster of ET cases ( $n = 9$ ) in the Wilkes-Barre area in space, but not in space and time. The low case participation and case chart review rates may have led to sensitivity and PPV with wide confidence intervals and hampered our ability to identify statistically significant disease clustering.

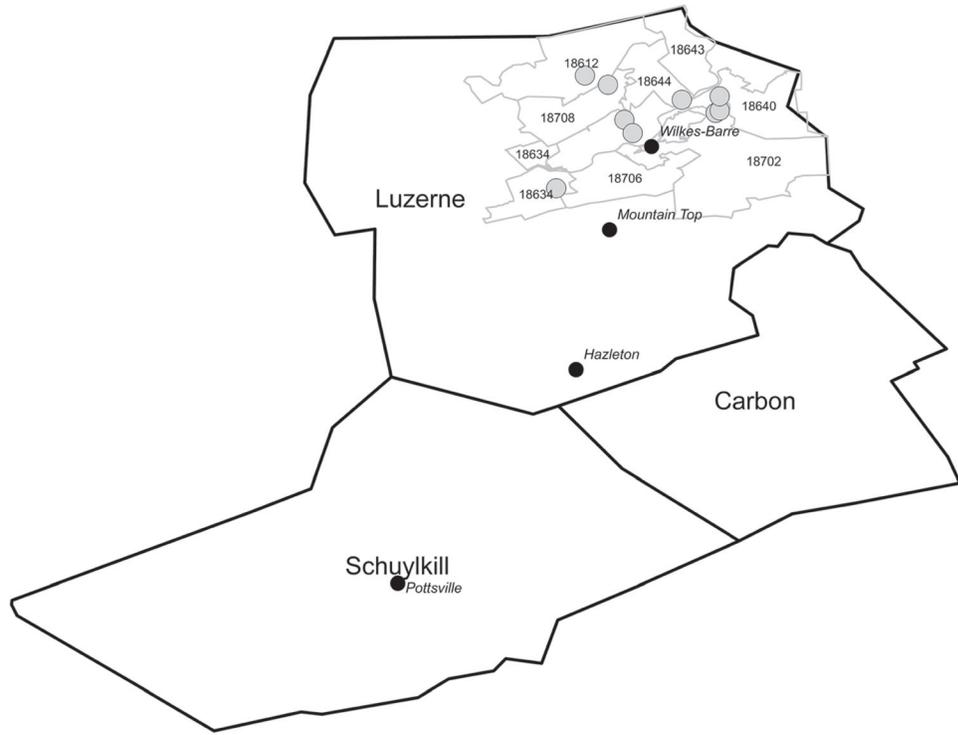
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**Figure 1.**  
Study Participation Flow Chart Final MPN Study Case Ascertainment



**Figure 2.** True ET Cases in the Tri-county Area ET Cluster ZIP Codes and Location of True ET Cases

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Table 1

## Case Ascertainment by Histology

Histology	PCR		Casefinding		Self-Report		Total	
	No.	%	No.	%	No.	%	No.	%
PV <sup>a</sup>	110	91.7	6	5.0	4	3.3	120	100.0
ET <sup>b</sup>	84	84.8	14	14.1	1	1.0	99	100.0
PMFC	29	93.5	2	6.5	0	0.0	31	100.0
APMF <sup>d</sup>	4	80.0	1	20.0	0	0.0	5	100.0
MPN/NOS <sup>e</sup>	33	94.3	2	5.7	0	0.0	35	100.0
Total	260	89.7	25	8.6	5	1.7	290	100.0

<sup>a</sup> Polycythemia vera, histology code 9950.

<sup>b</sup> Essential thrombocytopenia, histology code 9962.

<sup>c</sup> Primary myeloid fibrosis, histology code 9961.

<sup>d</sup> Acute panmyelosis with myelofibrosis, histology code 9931.

<sup>e</sup> Myeloproliferative neoplasm, not otherwise specified, histology code 9960.

Table 2

## Expert Panel Determination by Histology

Histology	Expert Panel Determination											
	Total		True Case			False Case			Indeterminate Case			
	No.	%	No.	%	95% CI (%)	No.	%	95% CI (%)	No.	%	95% CI (%)	
PV <sup>a</sup>	23	100.0	7	30.4	14.6–57.0	11	47.8	21.8–66.0	5	21.7	8.2–47.2	
ET <sup>b</sup>	13	100.0	9	69.2	34.9–90.1	0	0.0	0.0–26.5	4	30.8	9.9–65.1	
PMF <sup>c</sup>	3	100.0	1	33.3	0.8–90.6	2	66.7	9.4–99.2	0	0.0	0.0–70.8	
APMF <sup>d,e</sup>	0	–	0	–	–	0	–	–	0	–	–	
MPN/NOS <sup>f</sup>	5	100.0	3	60.0	14.7–94.7	1	7.1	0.5–71.6	1	10.0	0.5–71.6	
Study Total	44	100.0	20	45.5	30.7–62.6	14	31.8	16.1–45.5	10	22.7	12.4–40.3	

<sup>a</sup>Polycythemia vera, histology code 9950.

<sup>b</sup>Essential thrombocytopenia, histology code 9962.

<sup>c</sup>Primary myeloid fibrosis, histology code 9961.

<sup>d</sup>Acute panmyelosis with myelofibrosis, histology code 9931.

<sup>e</sup>One APMF case identified through PCR enhanced case finding was reviewed for PMF diagnosis based upon investigator judgment and determined to be a true PMF case.

<sup>f</sup>Myeloproliferative neoplasm, not otherwise specified, histology code 9960.

**Table 3**  
Expert Panel Reason for Determination of “Indeterminate” or “False” Case Status

<i>EP Reason</i>	<i>Indeterminate</i>		<i>False</i>		<i>Total</i>	
	No.	%	No.	%	No.	%
Not enough information/incomplete medical records	7	70.0	3	21.4	10	41.7
Non-MPN diagnosis	2	20.0	9	64.3	11	45.8
Other cancer	1	50.0	1	11.1	2	18.2
Secondary polycythemia	1	50.0	5	55.6	6	54.5
Other noncancer	0	0.0	3	33.3	3	27.3
Other MPN diagnosis	1	10.0	2	14.3	3	12.5
Total	10	100.0	14	100.0	24	100.0

**Table 4**

Sensitivity and Positive Predictive Value of Original PCR Data by Histology

Histology	"True" Cases Reported	"True" Cases Not Reported <sup>a</sup>	"False" Cases Reported <sup>b</sup>	Completeness <sup>c</sup>		Accuracy <sup>d</sup>	
				%	95% CI (%)	%	95% CI (%)
PV <sup>e</sup>	7	0	8	100.0	59.0–100.0	46.7	19.8–70.1
ET <sup>f</sup>	7	2	0	77.8	47.3–99.7	100.0	59.0–100.0
PMF <sup>g,h</sup>	0	1	2	0.0	0.0–97.5	0.0	0.0–84.2
MPN/NOS <sup>i</sup>	3	0	1	100.0	29.2–100.0	75.0	19.4–99.4
Study Total	17	3	11	85.0	66.9–98.7	60.7	38.9–76.5

<sup>a</sup>Cases that should have been included in the original PCR data set.

<sup>b</sup>Cases incorrectly reported to the PCR.

<sup>c</sup>True cases reported/(True cases reported + True cases not reported).

<sup>d</sup>True cases reported/(True cases reported + False cases reported).

<sup>e</sup>Polycythemia vera, histology code 9950.

<sup>f</sup>Essential thrombocytopenia, histology code 9962.

<sup>g</sup>Primary myeloid fibrosis, histology code 9961.

<sup>h</sup>One APMF case identified through PCR case finding was reviewed for PMF diagnosis based upon investigator judgment and determined to be true PMF case.

<sup>i</sup>Myeloproliferative neoplasm, not otherwise specified, histology code 9960.

**Table 5**

PV and Other MPN Original and Updated Average Annual Incidence Rates

Histology	Incidence Rates in the Tri-County Area Corrected for Sensitivity and Positive Predictive Value of Reporting									
	Original PCR Cases					Correction Factors				
	No.	Original Incidence Rate		Sensitivity		Positive Predictive Value (PPV)		Updated Incidence Rate (Original Incidence Rate / Sensitivity x PPV)		Estimated Rate Interval
		%	95% CI	%	95% CI	%	95% CI	Estimated Rate		
	<b>2006–2009</b>									
PV <sup>a</sup>	112	5.3	100.0%	59.0–100.0%	46.7%	14.6–57.0%	2.5		0.8–5.1	
	<b>2001–2009</b>									
ET <sup>b</sup>	85	1.8	77.8%	47.3–99.7%	100.0%	34.9–100.0%	2.3		0.6–3.8	
PMF <sup>c,d</sup>	29	0.6	0.0%	0.0–97.5%	0.0%	0.8–90.6%	0.0		0.0–0.5	
MPN/NOS <sup>e</sup>	33	0.7	100.0%	29.2–100.0%	75.0%	14.7–94.7%	0.5		0.1–2.3	
Study Total	259	8.4	89.5%	66.9–98.7%	58.6%	30.7–62.6%	5.5		2.6–7.9	

<sup>a</sup>Polycythemia vera, histology code 9950.

<sup>b</sup>Essential thrombocytopenia, histology code 9962.

<sup>c</sup>Primary myeloid fibrosis, histology code 9961.

<sup>d</sup>One APMF case identified through PCR case finding was reviewed for PMF diagnosis based upon investigator judgment and determined to be true PMF case.

<sup>e</sup>Myeloproliferative neoplasm, not otherwise specified, histology code 9960.