COLLEGE of AMERICAN PATHOLOGISTS

Supplemental Digital Content* | Methodology | March 2016

Bone Marrow Synoptic Reporting for Hematologic Neoplasms

Corresponding Author:
Cordelia Sever, MD, FCAP

Authors:
Carol Colasacco, MLIS, SCT(ASCP)
R. Bryan Rumble, MSc
Nicole E. Thomas, MPH, CT(ASCP)

http://www.archivesofpathology.org/doi/full/10.5858/arpa.2015-0450-SA

* The Supplemental Digital Content was not copyedited by *Archives of Pathology and Laboratory Medicine.*

METHODS USED TO PRODUCE THE GUIDELINE

Panel Composition

The College of American Pathologists (CAP) Pathology and Laboratory Quality Center (the Center) convened an expert panel (EP) consisting of pathologists, a hematologist/oncologist, and a methodologist consultant to develop an evidence-based guideline to formalize the basic components of a synoptic report for hematologic neoplasms. CAP approved the appointment of the project chair and panel members. The EP members performed the systematic evidence review. An advisory panel (AP) of pathologists, a hematologist/oncologist, and a molecular biologist also helped in the development of the guideline. The role of the AP members was to provide guidance and feedback on the key questions for the literature search, vet the draft guideline statements prior to the public comment period, and to review and provide feedback for the manuscript and supplemental digital content.

Conflict of Interest (COI) Policy

Prior to acceptance on the expert or advisory panel, potential members completed the CAP conflict of interest (COI) disclosure process, whose policy and form (in effect April 2010) require disclosure of material financial interest in, or potential for benefit of significant value from, the guideline's development or its recommendations 12 months prior through the time of publication. The potential members completed the COI disclosure form, listing any relationship that could be interpreted as constituting an actual, potential, or apparent conflict. The CAP Center uses the following criteria:

Nominees who have the following conflicts may be excused from the panel:

a. Stock or equity interest in a commercial entity that would likely be affected by the guideline or white paper
b. Royalties or licensing fees from products that would likely be affected by the guideline or white paper
c. Employee of a commercial entity that would likely be affected by the guideline or white paper

Nominees who have the following potentially manageable direct conflicts may be appointed to the panel:

a. Patents for products covered by the guideline or white paper
b. Member of an advisory board of a commercial entity that would be affected by the guideline or white paper
c. Payments to cover costs of clinical trials, including travel expenses associated directly with the trial
d. Reimbursement from commercial entity for travel to scientific or educational meetings

Everyone was required to disclose conflicts prior to beginning and continuously throughout the project's timeline. Expert panel members' disclosed conflicts are listed in the appendix of the manuscript. The CAP provided funding for the administration of the project; no industry funds were used in the development of the guideline. All panel members volunteered their time and were not compensated for their involvement, except for the contracted methodologist.

Literature Review and Analysis

The expert panel met 21 times through teleconference webinars from February 2, 2012 through March 31, 2015. Additional work was completed via electronic mail. The panel met in person November 2, 2013 to review evidence to date and draft recommendations.

Prior to the in-person meeting, the expert panel formed the following key questions for which to base the literature search:

1. Considering the possible primary bone marrow morphologic descriptors, which ones are required on a synoptic report if completeness is the outcome of interest?

2. Considering the possible ancillary studies that could be ordered on a bone marrow specimen, which ones are required on a synoptic report if completeness is the outcome of interest?
3. What sequence of results reporting should be followed?
   a. Considering the options available, is there an optimum report format that should be used if ease of use, error reduction, and fewer incompletes are the outcomes of interest?
   b. Is there an optimal presentation for the elements of the minimum data set if the outcomes of interest are clarity and ease of use?
4. Which components required for correct coding and data repositories should be included in the report?
   a. Coding
   b. Registries
   c. National guidelines (e.g., National Comprehensive Cancer Network [NCCN][1])
   d. Physician payment incentive requirements (e.g., Physician Quality Reporting System [PQRS][2])
5. What clinical or laboratory information should be included in the report?

All expert panelists participated in the systematic evidence review (SER). Each level of the SER (title-abstract, full text review, and data extraction) was performed in duplicate by two members of the expert panel. All expert panelists and a contracted methodologist performed adjudication of the conflicts. Articles meeting the inclusion criteria were assessed for strength of evidence, methodological rigor, and confirmation of validity by the methodologist. Supplemental Figure 1 displays the results of the literature review. All articles were available as discussion or background references. All members of the expert panel participated in developing draft recommendations, reviewing open comment feedback, finalizing and approving final recommendations and writing/editing of the manuscript.

Peer Review

An open comment period was held from April 21 through May 19, 2014 on the CAP Web site www.cap.org. Ten draft recommendations and two demographic questions were posted for peer review. An announcement was sent to the following societies deemed to have interest:

- CAP Board of Governors, Councils, Committees and Membership
- American Society for Clinical Pathology (ASCP)
- American Society of Hematology (ASH)
- Society for Hematopathology
- American Society for Clinical Oncology (ASCO)
- Association for Molecular Pathology (AMP)
- International Society for Laboratory Hematology (ISLH)
- European Association for Hematopathology (EAHP)
- European Society for Medical Oncology (ESMO)
- United States & Canadian Academy of Pathology (USCAP)
- Clinical Cytometry Society (CCS)
- American College of Medical Genetics (ACMG)

“Agree” and “Disagree” responses were captured for every proposed recommendation. The website also received 178 written comments. All ten draft recommendations achieved more than 80% agreement. Each expert panel member was assigned three pages of comments to review and summarize. After consideration of the comments, two draft recommendations were maintained with the original language; six were revised, and two draft recommendations were combined into one (i.e., one recommendation was dropped) for a total of nine final recommendations. Resolution of all changes was obtained by majority consensus of the panel using nominal group technique (rounds of teleconference webinars, email discussion and multiple edited recommendations) amongst the panel members. The final recommendations were approved by the expert panel with a formal vote. The panel considered

laboratory efficiency and feasibility throughout the entire considered judgment process.[3] Neither formal cost analysis nor cost effectiveness models were performed.

An independent review panel (IRP) was assembled to review and approve the guideline. The IRP was masked to the expert panel and vetted through the COI process.

Dissemination Plans

CAP plans to host a Bone Marrow Synoptic Reporting resource page which will include a link to the manuscript and supplement; a summary of the recommendations, a teaching PowerPoint and a frequently asked question (FAQ) document. The guideline will be promoted and presented at various society meetings.

Systematic Evidence Review (SER)

The objective of the SER was to determine the components required to create a complete bone marrow synoptic report. If of sufficient quality, findings from this review could provide an evidence base to support the development of the guideline. The scope of the SER and the key questions (KQs) were established by the EP in consultation with the methodologist prior to beginning the literature search.

Search and Selection

A systematic literature search for relevant evidence that was published between January 2002 and November 2012 was completed in the MEDLINE database utilizing both OvidSP (11/30/2012) and PubMed(12/5/2012). Three separate OvidSP search strategies were designed to address specific research questions. The search strings included medical subject headings (MeSH) and text words to capture the general concepts of bone marrow samples, specific benign and malignant hematologic entities, ancillary studies, and pathology reporting. The Ovid search strategies were adapted for PubMed. A separate literature search utilizing PsychINFO (11/26/12) was completed to identify articles that addressed the concepts of reading comprehension, communication, and clarity. No date parameters were set for the PsychINFO search. An update of the OvidSP and PsychINFO searches was conducted(7/9/2014) to identify relevant studies published through June 2014. The Ovid search strategy is included as Supplemental Figure 2.

All searches were limited to human studies published in English, and a publication filter was applied to the OvidSP and PubMed searches to exclude less rigorous studies as well as letters, commentaries and editorials.

Database searches were supplemented by a search for grey literature utilizing the Cochrane Library, TRIP database, Grey Literature Report, and Google Scholar. Meeting abstracts (January 2011-December 2012) from relevant pathology organizations (American Society of Hematology (ASH), American Society for Clinical Pathology (ASCP), College of American Pathologists (CAP) and United States and Canadian Academy of Pathology (USCAP)) were reviewed, and a focused handsearch (January 2011-December 2012) of selected pathology journals (*Archives in Pathology and Laboratory Medicine, American Journal of Clinical Pathology, American Journal of Surgical Pathology, Blood, Histopathology,* and *Modern Pathology*) was completed.

Reference lists of included articles were reviewed for relevant reports.

Selection at all levels was based on predetermined inclusion/exclusion criteria.
Included were:

- Human studies
- Studies published in English
- Comparative studies or a summary paper of comparative studies
- Studies that addressed at least one of the following:
    - Bone marrow samples used to diagnose one of the following conditions:
        - Multiple myeloma

    - Amyloidosis
    - Acute myeloid leukemia/Acute lymphoblastic leukemia
    - Chronic myelogenous leukemia
    - Primary myelofibrosis
    - Chronic myeloproliferative neoplasms
    - Myelodysplastic syndromes – clinical terms (e.g., low risk, high risk, World Health Organization (WHO)-refractory anemias)
    - Myelodysplastic/Myeloproliferative diseases
    - Hodgkin lymphoma
    - Non-Hodgkin lymphoma
    - Chronic lymphocytic leukemia
    - Anemia of chronic inflammation
    - Parvovirus B19
    - Iron deficiency anemia
    - Vitamin B12 deficiency
    - Folate deficiency
    - Paget's disease of the bone
    - Idiopathic immune thrombocytopenia
    - Aplastic anemia
  - Ancillary testing in bone marrow samples
  - The completeness of bone marrow reports by addressing morphologic descriptors
  - Optimum report formats to facilitate clarity, comprehension, and ease of use

Not included were:

- Non-English-language article/document or an English-language abstract or summary without a full article/document available in English.
- Animal studies
- Studies older than 2002
- Studies that addressed a neoplastic or non-neoplastic condition not defined in the inclusion criteria
- Non-comparative studies, letters, commentaries, editorials
- Studies that did not address at least one of the defined inclusion criteria

Outcomes of Interest

Due to the nature of the scope of this project, the outcomes of interest to the EP were not those typically associated with clinical guidelines (e.g., disease free survival, prognosis, overall survival, etc.) Instead, completeness of data fields and the report were outcomes of interest.

Data Extraction & Management

The data elements from an included article/document were extracted by one reviewer into standard data formats and tables developed using systematic review database software (DistillerSR, Evidence Partners Inc., Ottawa, Canada); a second reviewer confirmed accuracy and completeness. Any discrepancies in data extraction were resolved by discussion. A bibliographic database was established in EndNote (Thomson Reuters, Carlsbad, CA) to track all literature identified and reviewed during the study.

Quality Assessment Methods

An assessment of the quality of the evidence was performed for all retained studies following application of the inclusion and exclusion criteria. Using this method, studies deemed to be of low quality would not be excluded from the systematic review, but would be retained and their methodological strengths and weaknesses discussed where relevant. Studies would be assessed by confirming the presence of items related to both internal and external validity, and which are all associated with methodological rigor and a decrease in the risk of bias. These items were assessed as being either yes, no, partial, not reported (NR), or not applicable (N/A) in the following way:

Clinical Practice Guidelines (CPGs) and Systematic Reviews (SRs) were assessed for quality by confirming the following attributes were considered and incorporated in its design as recommended by the Institute of Medicine (IOM).[4] (Summarized in Supplemental Table 1)

- Based on a systematic review (this was not assessed for SRs)
- Included a multidisciplinary panel
- Patient preferences were considered
- Important patient sub-types were considered
- Methods were well-described and reproducible
- Information on potential conflicts of interest were gathered and disclosed
- Quality of the evidence was assessed
- Strength of the evidence was rated
- CPG includes a plan for updating
- Sources of funding are disclosed

Meta-analyses (MAs) were assessed in a similar fashion to CPGs according to the following criteria:

- Based on a systematic review
- Methods were well-described and reproducible
- Quality of the evidence was assessed
- Any planned pooling was stated a priori
- Limitations of the analysis are discussed
- Sources of funding are disclosed

Randomized Control Trials (RCTs) and Quasi-RCTs were assessed for quality according to reporting and full description of:

- Randomization method fully-described
- Details on any blinding was provided
- Provided details of all planned analyses
- Stated the expected effect size and described the statistical power calculation
- Reported the length of follow-up
- Provided a description of the baseline characteristics for all patients by treatment/assessment arm
- Sources of funding are disclosed

Non-randomized clinical trials (NRCTs), prospective cohort studies (PCS), and retrospective cohort studies (RCS) were assessed according to:

- Balance between treatment/assessment groups
- Reporting of baseline characteristics
- Reporting if any adjustments were made where baseline differences were detected
- Sources of funding

Supplemental Table 1 summarizes the quality assessment criteria by study design.

Each study was assessed individually, and then each study type was summarized. Finally, a summary of the overall quality of the evidence was given considering the evidence in totality.

Quality Assessment Results

A total of 95 studies[5-99] were retained, comprising 2 CPGs,[5, 12] 1 SR,[13] 2 RCTs,[6, 14] 1 quasi-RCT,[9] 7 non-RCTs,[7, 8, 11, 24, 26-28] 39 PCS,[10, 15-23, 25, 29-31, 33-56, 65] and 43 RCS[32, 57-64, 66-99] which makes up the body of evidence in this systematic review. All included studies were assessed for quality.

Statement 1 was supported by 11 studies,[6, 57, 58, 61, 62, 71, 72, 74-76, 91] comprising one RCT[6] and 10 RCS.[57, 58, 61, 62, 71, 72, 74-76, 91] Risk of bias assessment scores were either low-moderate (N=5) or moderate-high

(N=5). The single RCT[6] was well-reported but did not disclose any information on blinding, baselines differences in the patient populations, or details of the expected effect size and the power calculation. Of the 10 RCS, only three reported a balance between groups,[61, 62, 76] and three reported on baseline characteristics and any differences.[72, 75, 76] None of the studies reported industry funding. Overall, none of the studies providing the evidence base for statement 1 were found to have methodological flaws that would raise concerns about the studies' findings. Refer to Supplemental Table 2 for the quality assessment results of the included studies for statement 1.

Statement 2 was supported by six studies,[10, 54, 64, 67, 87, 88] comprising two PCS[10, 54] and four RCS.[64, 67, 87, 88] Risk of bias assessment scores ranged from low-moderate[64, 88] to moderate-high.[10, 87] Of the two PCS, one[10] reported on baseline characteristics and differences between the groups, while the other[54] only reported partial differences. The study by List et al[10] reported industry funding. Of the four RCS, one[87] fully reported on baseline characteristics and differences between groups, although the other three partially reported on this.[64, 67, 88] The study by Kvasnicka et al[67] reported industry funding while the study reported by Greenberg et al[87] reported at least partial industry funding. Overall, none of the studies providing the evidence base for statement 2 were found to have methodological flaws that would raise concerns about the studies' findings. Refer to Supplemental Table 3 for the quality assessment results of the included studies for statement 2.

Statement 3 was supported by 13 studies,[15, 24, 27, 29, 50, 54, 60, 64, 68, 88, 90, 92, 95] comprising two NRCT,[24, 27] four PCS,[15, 29, 50, 54] and seven RCS.[60, 64, 68, 88, 90, 92, 95] Risk of bias scores were either low-moderate,[24, 27, 29, 64, 88, 90, 95] moderate,[15, 50, 54] or moderate-high.[60, 68, 92] Both[24, 27] of the NRCT reported on baseline characteristics and differences between groups and neither reported on industry-funding. For the PCS, two[29, 50] reported on baseline characteristics and differences, and one[54] partially reported this. None of the PCS reported industry funding. For the RCS, four[60, 68, 92, 95] reported on baseline characteristics and differences between groups, and three[64, 88, 90] partially reported on this. One of the RCS, the study reported by Luigi et al[68] reported industry funding. Overall, none of the studies providing the evidence base for statement 3 were found to have methodological flaws that would raise concerns about the studies' findings. Refer to Supplemental Table 4 for the quality assessment results of the included studies for statement 3.

Statement 4 was supported by 12 studies,[8, 20, 27, 50, 51, 54, 59, 63, 67, 68, 87, 95] comprising two NRCT,[8, 27] four PCS,[20, 50, 51, 54] and six RCS.[59, 63, 67, 68, 87, 95] Risk of bias scores ranged from low-moderate[8, 27, 51, 63, 95] to moderate-high.[20, 87] One of two NRCT[27] fully reported on baseline characteristics and differences between groups while the study by Hultdin et al[8] only partially reported on that, however that same study did report adjustments to the analysis were made based on any detected differences. Neither of these studies reported any industry funding. Of the four PCS, three[20, 50, 51] reported on baseline characteristics and differences between groups while the fourth[54] partially reported on this. The study by Campbell et al[20] reported industry funding. For the RCS studies, four[63, 68, 87, 95] reported on baseline characteristics and differences between groups while the other two[59, 67] partially reported on that. Two[67, 68] reported industry funding and another[87] reported at least partial industry funding. Overall, none of the studies providing the evidence base for statement 4 were found to have methodological flaws that would raise concerns about the studies' findings. Refer to Supplemental Table 5 for the quality assessment results of the included studies for statement 4.

Statement 5 was supported by 20 studies,[9, 11, 18, 19, 21, 25, 26, 28, 31, 32, 34-38, 43, 53, 55, 80, 100] 19 of which were included in the systematic review and were assessed for risk of bias.[9, 11, 18, 19, 21, 25, 26, 28, 31, 32, 34-38, 43, 53, 55, 80] The studies comprised one QRCT,[9] three NRCT,[11, 26, 28] 13 PCS,[18, 19, 21, 25, 31, 34-38, 43, 53, 55] and two RCS.[32, 80] Risk of bias scores ranged from low-moderate[18, 19, 25, 36, 37, 55, 80] to moderate-high.[34, 35, 38] The single QRCT[9] only partially reported on differences in patient characteristics, and reported no industry funding. Of the three NRCT,[11, 26, 28] two[26, 28] reported on baseline characteristics and differences between groups, while the other[11] partially reported on that. The trial by Martinelli et al[11] reported partial industry funding. Of the 12 PCS, six[18, 21, 35, 37, 38, 55] reported on baseline characteristics and differences between groups, and three others[19, 31, 34] reported on that partially. Three PCS[34, 35, 38] reported at least partial industry funding. Of the two RCS, one[80] reported on baseline characteristics and differences between groups and the other[32] reported partial industry funding. Overall, none of the studies providing the

evidence base for statement 5 were found to have methodological flaws that would raise concerns about the studies' findings. Refer to Supplemental Table 6 for the quality assessment results for the included studies for statement 5.

Statement 6 was supported by 42 studies,[8-11, 13, 15, 18-21, 24-29, 31, 32, 34-38, 43, 50, 51, 53-55, 59, 60, 63, 64, 67, 68, 80, 87, 88, 90, 92, 95, 100] 40[8, 9, 11, 13, 15, 18-21, 24-29, 31, 32, 34-38, 43, 50, 51, 53-55, 59, 60, 63, 64, 67, 68, 80, 87, 88, 90, 92, 95] of which were included in the systematic review and were assessed for risk of bias. These studies comprised one systematic review,[13] one QRCT,[9] six NRCT,[8, 11, 24, 26-28] 19 PCS,[15, 18-21, 25, 29, 31, 34-38, 43, 50, 51, 53-55] and 13 RCS.[32, 59, 60, 63, 64, 67, 68, 80, 87, 88, 90, 92, 95] Risk of bias scores ranged from low-moderate[8, 13, 18, 19, 24, 25, 27, 29, 36, 37, 51, 55, 63, 64, 80, 88, 90, 95] to moderate-high.[20, 34, 35, 38, 60, 87, 92]
The systematic review[13] had a risk of bias assessment score of low-moderate. Despite deficits in the reporting of the methods used in this systematic review, including panel composition, no patient input, only partial description of the methods used, no quality assessment for included papers, no strength of evidence scoring, and no reporting on the source of funding, no penalties were allocated due to the nature of the topic and the low risk of any biases negatively impacting any patient outcomes. The single QRCT[9] only partially reported on differences in patient characteristics. Of the six NRCTs, four[24, 26-28] baseline characteristics and differences between groups, and two[8, 11] reported that partially. One[8] reported making adjustments when these differences were detected, and another[11] reported partial industry funding. Of the 19 PCS, 10[18, 20, 21, 29, 35, 37, 38, 50, 51, 55] reported on baseline characteristics and differences between groups, and four[19, 31, 34, 54] partially reported on that. One[20] reported industry funding and another three[34, 35, 38] reported at least partial industry funding. For the RCS, seven[60, 63, 68, 80, 87, 92, 95] fully reported on baseline characteristics and differences between groups and another five[59, 64, 67, 88, 90] partially reported on that. Two[67, 68] reported industry funding and another two[32, 87] reported at least partial industry funding. Overall, none of the studies providing the evidence base for statement 6 were found to have methodological flaws that would raise concerns about the studies' findings. Refer to Supplemental Table 7 for the quality assessment results for the included studies for statement 6.

Statement 7 was supported by one systematic review, reported by Valenstein et al.[13] This systematic review had a risk of bias assessment score of low-moderate. Despite deficits in the reporting of the methods used in this systematic review, including panel composition, no patient input, only partial description of the methods used, no quality assessment for included papers, no strength of evidence scoring, and no reporting on the source of funding, no penalties were allocated due to the nature of the topic and the low risk of any biases negatively impacting any patient outcomes. Overall, this single paper that provided the evidence base for statement 7 was found to have no methodological flaws that would raise concerns about its findings. Refer to Supplemental Table 8 for the quality assessment results for the included studies for statement 7.

No studies were included for statement 8.

Statement 9 was supported by 11 studies,[7, 10, 27, 31, 54, 63, 64, 67, 87, 88, 101] 10 of which were included in the systematic review and were assessed for risk of bias.[7, 10, 27, 31, 54, 63, 64, 67, 87, 88] These studies comprised two NRCT,[7, 27] three PCS,[10, 31, 54] and five RCS.[63, 64, 67, 87, 88] Risk of bias scores ranged from low-moderate[27, 63, 64, 88] to moderate-high.[10, 87] Both of the two NRCTs[7, 27] reported on baseline characteristics and differences between groups, and one[7] reported industry funding. Of the three PCS, only one[10] reported on baseline characteristics and differences between groups, with two[31, 54] reporting on that partially. One PCS[10] reported industry funding. Of the five RCS, two[63, 87] reported on baseline characteristics and differences between groups, and three[64, 67, 88] reported that partially. One[67] reported industry funding and another[87] reported partial industry funding. Overall, none of the studies providing the evidence base for statement 9 were found to have methodological flaws that would raise concerns about the studies' findings. Refer to Supplemental Table 9 for the quality assessment results for the included studies for statement 9.

Assessing the Strength of Recommendations

The central question that the panel addressed in developing the guideline was "For hematologic neoplasms, should synoptic reports be used and what elements should be included to render a complete report?"

Development of recommendations required that the panel review the identified evidence and make a series of key judgments:

1) What are the significant findings related to each KQ or outcome? Determine any regulatory requirements and/or evidence that support a specific action.
2) What is the overall strength of evidence supporting each KQ or outcome? Strength of evidence is graded as Convincing, Adequate or Inadequate, based on four published criteria (Supplemental Table 10). Strength of evidence is a key element in determining the strength of a recommendation.
3) What is the strength of each recommendation? There are many methods for determining the strength of a recommendation based on the strength of evidence and the magnitude of net benefit or harm. However, such methods have rarely (if ever) been applied to the area of synoptic reporting. Therefore, the method for determining strength of recommendation has been modified for this application (Supplemental Table 11), and is based on the strength of evidence and the likelihood that further studies will change the conclusions. Recommendations not supported by evidence (i.e., evidence was missing or insufficient to permit a conclusion to be reached) were made based on consensus expert opinion. Another potential consideration is the likelihood that additional studies will be conducted that fill gaps in knowledge.
4) What is the net balance of benefits and harms? The consideration of net balance of benefits and harms will focus on the core recommendation that synoptic reports should be adopted as a component of bone marrow pathology reports.

Discussion of Benefits and Risks of Implementing the Recommendations

Statement 1: Laboratories should adopt synoptic reporting as a component of bone marrow pathology reports for clearly defined neoplasia or widely applied classification schemes and receive appropriate institutional support.

Supplemental Table 12 summarizes studies' findings in support of the superiority of synoptic reporting over unstructured, narrative reports.

Based on the feedback of various pathologist stakeholders, the Center deemed the topic of synoptic reporting for hematologic neoplasms a priority concern. The benefits of implementing synoptic reports for bone marrow pathology reports include standardization of reporting, ease of comprehension, consistency, completeness/thoroughness, reproducibility, availability of data for downstream use, and the ability for cross-institutional comparable reporting. Ultimately the expert panel believes that these factors will improve the overall quality of patient care.
The cost and time involved in creating/implementing synoptic reporting systems might pose a challenge for some institutions. Nonetheless, the panel concludes that the balance between the desirable and undesirable effects is in favor of synoptic reporting.

Statement 2: When reporting peripheral blood specimens for bone marrow synoptic reports, laboratories should report clinically and diagnostically pertinent elements, if available. These key elements may include one or more complete blood cell count parameters, absolute cell counts and relevant morphologic descriptors.

Statement 3: When reporting bone marrow aspirate results, laboratories should report clinically and diagnostically pertinent elements in the synoptic section. These key elements may include the evidence-based parameters such as blast percentage, dyspoiesis, myeloid:erythroid ratio, morphology of myeloid/lymphoid elements, and enumeration of lymphoid elements and plasma cells; additional elements may be included in nonsynoptic sections of the report.

Statement 4: When reporting bone marrow core biopsy results, laboratories should report clinically or diagnostically pertinent elements in the synoptic section. These key elements may include the evidence-based parameters such as fibrosis, cellularity, distribution pattern of hematopoietic elements, morphology of lymphoid elements, and enumeration of lymphoid elements and plasma cells; additional elements may be included in nonsynoptic sections of the report.

Refer to Supplemental Tables 13-15 for study data by outcome of significance for peripheral blood specimens, bone marrow aspirates, and bone marrow core biopsies respectively.

For statements 2, 3, and 4, there are similar benefits: standardization of reportable elements for diagnosis, prognosis and therapeutic decision-making, and availability of data for downstream use. While the systematic review of the literature identified evidence-based morphologic descriptors specific to each recommendation, the expert panel recognized that there might be a number of scenarios for which a different descriptor might be included. The panel agreed that it was important that these recommendations allowed for some flexibility to accommodate such scenarios.

Statement 5: If relevant ancillary testing studies are performed on the primary sample (blood or bone marrow), laboratories should report the results, general methodology, performance site and interpretation site or have the data be readily available. If the results are not available, pending status should be explicitly stated.

Supplemental Table 16 summarizes studies' findings.

For samples that go on to have ancillary testing, capturing the aforementioned items would aid in identifying the diagnostic and/or prognostic information and data used for targeted therapies. This information would then be available for downstream use. The expert panel acknowledges that timeliness in reporting might be delayed. Some ancillary tests may need to be released before the full report is available. The panel concurred that indicating pending status would be beneficial to pathologists and other various stakeholders checking the report, as treatment options my change based on ancillary test results. While there might be increased costs in adding critical ancillary data to the synoptic report, the costs that might incur were deemed to be small relative to the net benefits of the information provided.

Statement 6: Laboratories should include in the synoptic section of the report, data groups for diagnosis, supporting studies, and ancillary data that are critical for diagnosis. Key morphologic descriptors should be included and may be in the diagnosis line if critical or if a component of the disease classification. The diagnosis (or diagnosis group) should head the synoptic section when possible. A narrative interpretative comment should immediately follow the synoptic section if required.

This recommendation builds upon previously established standards for synoptic reporting.[102] The benefits include efficient transmission of information/data, and standardized reporting within an institution. A standardized synoptic report would likely lead to increased speed in reading the report, due to the consistent nature. Since interpretive comments would follow the synoptic section, clinicians would not likely have to sift through the more lengthy narrative to try to determine key information. As a result of standardizing the synoptic report, one might experience inconvenience in transcribing the report or a lack of autonomy. The expert panel believes that the value of standardization outweighs these inconveniences.

Statement 7: Laboratories should consider the integrity of electronic data transmission for formatting and data presentation of synoptic reports.

The benefits of implementing this recommendation include improved comprehension of the report and efficient transmission of data. No harms were identified for this recommendation.

Statement 8: No recommendation is made regarding the inclusion of coding terms in a synoptic report since coding terms are distinct from scientific terms and vary considerably among health authorities, payers, and different countries.

The evidence was insufficient to inform the initial key question "Which components required for correct coding and data repositories should be included in the report," therefore no recommendation is made.

Statement 9: Laboratories should include clinical and laboratory data required for a definitive diagnosis in the synoptic section, along with its source(s), if applicable. Supplemental Table 17 summarizes studies' findings.

Including relevant clinical and laboratory information results in the completeness of the report and aids the pathologist in making a definitive diagnosis. The time associated with including this information is considerable. The variability of data available to pathologists is high and it would not be feasible for the pathologist to be the initiator of including the clinical information. The expert panel therefore concludes that the clinician should be responsible for transmitting clinical information. While there may be pushback from clinicians to provide this information due to time constraints or other reasons, the feedback the expert panel received during open comment period suggests that pathologists find it acceptable that clinicians take ownership of this initial step and that the pathologists helps support this task.

Supplemental Table 1 – Quality Assessment Criteria by Study Design

Criteria	**Study Design**			
	Clinical Practice Guideline (CPG)/Systematic Review (SR)	**Meta-analyses**	**Randomized Control Trial (RCT)/Quasi-randomized Controlled Trial (QRCT)**	**Non-randomized Controlled Trial (NRCT)/Prospective Cohort Study (PCS) /Retrospective Control Study (RCS)**
Based on a systematic review	✓ (CPG only)	✓		
Included a multidisciplinary panel	✓			
Patient preferences were considered	✓			
Important patient sub-types were considered	✓			
Methods were well-described and reproducible	✓	✓		
Information on potential conflicts of interest were gathered and disclosed	✓			
Quality of the evidence was assessed	✓	✓		
Strength of the evidence was rated	✓			
CPG includes a plan for updating	✓			
Sources of funding are disclosed	✓	✓	✓	✓
Any planned pooling was stated a priori		✓		
Limitations of the analysis are discussed		✓		

Randomization method fully-described			✓	
Details on any blinding was provided			✓	
Provided details of all planned analyses			✓	
Stated the expected effect size and described the statistical power calculation			✓	
Reported the length of follow-up			✓	
Provided a description of the baseline characteristics for all patients by treatment/assessment arm			✓	✓
Balance between treatment/assessment groups				✓
Reporting if any adjustments were made where baseline differences were detected				✓

Supplemental Table 2 – Quality Assessment Results for Statement 1

Randomized Controlled Trials (N=1)									
Author	**Year**	**Provided details on randomization**	**Provided details on blinding**	**Provided details on any planned analysis**	**Expected effect size calculation and power calculation**	**Reported on length of follow-up**	**Reported on any differences in patient characteristics**	**Funding source**	**Overall risk of bias assessment**
Branston et al,[6]	2002	Yes (Y)	No (N)	Y	N	Y	Not Applicable (N/A)	Non-industry	Low-moderate

Retrospective Cohort Studies (N=10)						
Author	**Year**	**Was there balance between treatment/assessment**	**Reporting of baseline characteristics (and any differences detected**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**

		groups?	**between groups)**			
Beattie et al,[61]	2003	Y	N/A	N/A	Not reported (NR)	Moderate-high
Chan et al,[62]	2008	Y	N	N/A	NR	Moderate-high
Haugland et al,[74]	2011	N	N/A	N/A	Non-industry	Low-moderate
Messenger et al,[91]	2011	N	NR	N/A	Non-industry	Low-moderate
Austin et al,[58]	2009	N/A	N/A	N/A	Non-industry	Low-moderate
Harvey et al,[72]	2005	Partial	Y	NR	Non-industry	Low-moderate
Aumann et al[57]	2012	N/A	N/A	N/A	NR	Moderate-high
Gill et al,[71]	2009	Partial	N/A	NR	NR	Moderate-high
Idowu et al,[75]	2010	N/A	Y	N/A	NR	Moderate-high
Karim et al,[76]	2008	Y	Y	NR	Non-industry	Low-moderate

Supplemental Table 3 – Quality Assessment Results for Statement 2

Prospective Cohort Studies (N=2)

Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**

List et al,[10]	2006	Not applicable (N/A)	Yes (Y)	N/A	Industry	Moderate-high
Wang et al,[54]	2011	N/A	Partial	N/A	Not reported (NR)	Moderate
Retrospective Cohort Studies (N=4)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Gandemer et al,[64]	2009	N/A	Partial	N/A	Non-industry	Low-moderate
Kao et al,[88]	2008	N/A	Partial	N/A	Non-industry	Low-moderate
Kvasnicka et al,[67]	2006	N/A	Partial	N/A	Industry	Moderate
Greenberg et al,[87]	2012	N/A	Y	N/A	Partial-industry	Moderate-high

Supplemental Table 4 – Quality Assessment Results for Statement 3

Non-randomized Controlled Trials (N=2)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Jabbour et al,[24]	2006	Not applicable (N/A)	Yes (Y)	N/A	Not reported (NR)	Low-moderate
Lombardo et al,[27]	2002	N/A	Y	N/A	Non-industry	Low-moderate

Prospective Cohort Studies (N=4)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Wang et al,[54]	2011	N/A	Partial	N/A	NR	Moderate
Basso et al,[15]	2009	No (N)	N	NR	Non-industry	Moderate
Fernandez de Larrea et al,[29]	2011	N/A	Y	N/A	Non-industry	Low-moderate
Rowe et al,[50]	2010	N/A	Y	N/A	NR	Moderate
Retrospective Cohort Studies (N=7)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Gandemer et al,[64]	2009	N/A	Partial	N/A	Non-industry	Low-moderate
Kao et al,[88]	2008	N/A	Partial	N/A	Non-industry	Low-moderate
Baumann et al,[60]	2012	N/A	Y	N/A	NR	Moderate-high

Lugli et al,[68]	2005	N/A	Y	N/A	Industry	Moderate-high
Liu et al,[90]	2009	N/A	Partial	N/A	Non-industry	Low-moderate
Thiele et al,[95]	2011	N	Y	N	Non-industry	Low-moderate
Musolino et al,[92]	2010	N/A	Y	N/A	NR	Moderate-high

Supplemental Table 5 – Quality Assessment Results for Statement 4

Non-randomized Controlled Trials (N=2)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Lombardo et al,[27]	2002	Not applicable (N/A)	Yes (Y)	N/A	Non-industry	Low-moderate
Hultdin et al,[8]	2007	No (N)	Partial	Y	Non-industry	Low-moderate

Prospective Cohort Studies (N=4)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Wang et al,[54]	2011	N/A	Partial	N/A	Not reported (NR)	Moderate
Rowe et al,[50]	2010	N/A	Y	N/A	NR	Moderate

Campbell et al,[20]	2009	N/A	Y	N/A	Industry	Moderate-high
Takasaki et al,[51]	2007	N/A	Y	N/A	Non-industry	Low-moderate

Retrospective Cohort Studies (N=6)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Kvasnicka et al,[67]	2006	N/A	Partial	N/A	Industry	Moderate
Greenberg et al,[87]	2012	N/A	Y	N/A	Partial-industry	Moderate-high
Lugli et al,[68]	2005	N/A	Y	N/A	Industry	Moderate
Thiele et al,[95]	2011	N	Y	N	Non-industry	Low-moderate
Barbui et al,[59]	2012	N/A	Partial	N/A	Non-industry	Moderate
Gallamini et al,[63]	2004	N/A	Y	N/A	Non-industry	Low-moderate

Supplemental Table 6 – Quality Assessment Results for Statement 5

Quasi-randomized Control Trials (N=1)									
Author	**Year**	**Provided details on randomization**	**Provided details on blinding**	**Provided details on any planned analysis**	**Expected effect size calculation and power calculation**	**Reported on length of follow-up**	**Reported on any differences in patient characteristics**	**Funding source**	**Overall risk of bias assessment**

Irving et al,[9]	2009	No (N)	N	N	N	N	Partial	Non-industry	Moderate
Non-randomized Controlled Trials (N=3)									
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**				**Funding source**	**Overall risk of bias assessment**
Martinelli et al,[11]	2006	Not applicable (N/A)	Partial	N/A				Partial	Moderate
Liu et al,[26]	2012	N/A	Yes (Y)	N/A				Not reported (NR)	Moderate
Schlette et al,[28]	2009	N/A	Y	N/A				NR	Moderate
Prospective Cohort Studies (N=13)									
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**				**Funding source**	**Overall risk of bias assessment**
Bjorklund et al,[18]	2009	N/A	Y	N/A				Non-industry	Low-moderate
Bottcher et al,[19]	2008	N/A	Partial	N/A				Non-industry	Low-moderate
Chen et al,[21]	2011	N/A	Y	N/A				NR	Moderate
Langebrake et al,[25]	2006	N	NR	NR				Non-industry	Low-moderate
Kern et al,[31]	2003	N/A	Partial	N/A				NR	Moderate
Merx et al,[34]	2002	N/A	Partial	N/A				Partial industry	Moderate-high
Moreton et al,[35]	2005	N/A	Y	N/A				Partial industry	Moderate-high

Morgado et al,[36]	2012	N/A	N	N/A	Non-industry	Low-moderate
Perea et al,[37]	2005	N/A	Y	N/A	Non-industry	Low-moderate
Quintas-Cardama et al,[38]	2009	N/A	Y	N/A	Partial industry	Moderate-high
Vance et al,[53]	2007	N/A	N	N/A	NR	Moderate
Wiedswang et al,[55]	2003	N/A	Y	N/A	Non-industry	Low-moderate
Chopra et al,[43]	2012	Y	NR	NR	NR	Moderate
Retrospective Cohort Studies (N=2)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Lane et al,[80]	2008	N/A	Y	N/A	Non-industry	Low-moderate
Lundan et al,[32]	2008	N/A	N	N/A	Partial industry	Moderate

Supplemental Table 7 – Quality Assessment Results for Statement 6

Systematic Reviews (N=1)											
Author, RefID	**Year**	**Multi-disciplinary panel**	**Patient preferences considered**	**important patient sub-types considered**	**Well-described and reproducible methods**	**Conflicts of interest are examined**	**Rated quality of the evidence**	**Rated strength of the evidence**	**Includes a plan for updating**	**Funding source**	**Overall risk of bias assessment**
Valenstein[13]	2008	No (N)	Not applicable (N/A)	N/A	Partial	Not reported (NR)	N	N	N	NR	Low-moderate
Quasi-randomized Control Trials (N=1)											

Author	Year	Provided details on randomization	Provided details on blinding	Provided details on any planned analysis	Expected effect size calculation and power calculation	Reported on length of follow-up	Reported on any differences in patient characteristics	Funding source	Overall risk of bias assessment
Irving et al,[9]	2009	N	N	N	N	N	Partial	Non-industry	Moderate

Non-randomized Controlled Trials (N=6)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Jabbour et al,[24]	2006	N/A	Yes (Y)	N/A	NR	Low-moderate
Lombardo et al,[27]	2002	N/A	Y	N/A	Non-industry	Low-moderate
Hultdin et al,[8]	2007	N	Partial	Y	Non-industry	Low-moderate
Martinelli et al,[11]	2006	N/A	Partial	N/A	Partial	Moderate
Liu et al,[26]	2012	N/A	Y	N/A	NR	Moderate
Schlette et al,[28]	2009	N/A	Y	N/A	NR	Moderate

Prospective Cohort Studies (N=19)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Wang et al,[54]	2011	N/A	Partial	N/A	NR	Moderate
Basso et al,[15]	2009	N	N	NR	Non-industry	Moderate
Fernandez de Larrea et al,[29]	2011	N/A	Y	N/A	Non-industry	Low-moderate
Rowe et al,[50]	2010	N/A	Y	N/A	NR	Moderate

Campbell et al,[20]	2009	N/A	Y	N/A	Industry	Moderate-high
Takasaki et al,[51]	2007	N/A	Y	N/A	Non-industry	Low-moderate
Bjorklund et al,[18]	2009	N/A	Y	N/A	Non-industry	Low-moderate
Bottcher et al,[19]	2008	N/A	Partial	N/A	Non-industry	Low-moderate
Chen et al,[21]	2011	N/A	Y	N/A	NR	Moderate
Langebrake et al,[25]	2006	N	NR	NR	Non-industry	Low-moderate
Kern et al,[31]	2003	N/A	Partial	N/A	NR	Moderate
Merx et al,[34]	2002	N/A	Partial	N/A	Partial industry	Moderate-high
Moreton et al,[35]	2005	N/A	Y	N/A	Partial industry	Moderate-high
Morgado et al,[36]	2012	N/A	N	N/A	Non-industry	Low-moderate
Perea et al,[37]	2005	N/A	Y	N/A	Non-industry	Low-moderate
Quintas-Cardama et al,[38]	2009	N/A	Y	N/A	Partial industry	Moderate-high
Vance et al,[53]	2007	N/A	N	N/A	NR	Moderate
Wiedswang et al,[55]	2003	N/A	Y	N/A	Non-industry	Low-moderate
Chopra et al,[43]	2012	Y	NR	NR	NR	Moderate

Retrospective Cohort Studies (N=13)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Gandemer et al,[64]	2009	N/A	Partial	N/A	Non-industry	Low-moderate
Kao et al,[88]	2008	N/A	Partial	N/A	Non-industry	Low-moderate
Kvasnicka et al,[67]	2006	N/A	Partial	N/A	Industry	Moderate
Greenberg et al,[87]	2012	N/A	Y	N/A	Partial-industry	Moderate-high
Baumann et al[60]	2012	N/A	Y	N/A	NR	Moderate-high
Lugli et al,[68]	2005	N/A	Y	N/A	Industry	Moderate
Liu et al,[90]	2009	N/A	Partial	N/A	Non-industry	Low-moderate
Thiele et al,[95]	2011	N	Y	N	Non-industry	Low-moderate
Musolino et al,[92]	2010	N/A	Y	N/A	NR	Moderate-high
Barbui et al,[59]	2012	N/A	Partial	N/A	Non-industry	Moderate
Gallamini et al,[63]	2004	N/A	Y	N/A	Non-industry	Low-moderate
Lane et al[80]	2008	N/A	Y	N/A	Non-industry	Low-moderate
Lundan et al,[32]	2008	N/A	N	N/A	Partial industry	Moderate

Supplemental Table 8 – Quality Assessment Results for Statement 7

Systematic Reviews (N=1)											
Author, RefID	**Year**	**Multi-disciplinary panel**	**Patient preferences considered**	**Important patient sub-types considered**	**Well-described and reproducible methods**	**Conflicts of interest are examined**	**Rated quality of the Evidence**	**Rated strength of the evidence**	**Includes a plan for updating**	**Funding source**	**Overall risk of bias assessment**
Valenstein [13]	2008	No (N)	Not applicable (N/A)	N/A	Partial	Not reported (NR)	N	N	N	NR	Low-moderate

Supplemental Table 9 – Quality Assessment Results for Statement 9

Non-randomized Controlled Trials (N=2)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Lombardo et al,[27]	2002	Not applicable (N/A)	Yes (Y)	N/A	Non-industry	Low-moderate
Czuczman et al,[7]	2006	N/A	Y	N/A	Industry	Moderate
Prospective Cohort Studies (N=3)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
List et al,[10]	2006	N/A	Y	N/A	Industry	Moderate-high
Wang et al,[54]	2011	N/A	Partial	N/A	Not reported (NR)	Moderate
Kern et	2003	N/A	Partial	N/A	NR	Moderate

al,[31]						
Retrospective Cohort Studies (N=5)						
Author	**Year**	**Was there balance between treatment/assessment groups?**	**Reporting of baseline characteristics (and any differences detected between groups)**	**Reporting of any adjustment when differences were present**	**Funding source**	**Overall risk of bias assessment**
Gandemer et al,[64]	2009	N/A	Partial	N/A	Non-industry	Low-moderate
Kao et al,[88]	2008	N/A	Partial	N/A	Non-industry	Low-moderate
Kvasnicka et al,[67]	2006	N/A	Partial	N/A	Industry	Moderate
Greenberg et al,[87]	2012	N/A	Y	N/A	Partial-industry	Moderate-high
Gallamini et al,[63]	2004	N/A	Y	N/A	Non-industry	Low-moderate

Supplemental Table 10. Grades for Strength of Evidence

Convincing • Two or more Level 1[a] or 2 studies (study design and execution) that had an appropriate number and distribution of challenges[b] and reported consistent[c] and generalizable[d] results. • One Level 1 or 2 study that had an appropriate number and distribution of challenges and reported generalizable results.
Adequate • Two or more Level 1 or 2 studies that lacked the appropriate number and distribution of challenges OR were consistent but not generalizable.
Inadequate • Combinations of Level 1 or 2 studies that show unexplained inconsistencies OR combinations of one or more lower quality studies (Level 3 or 4) OR expert opinion.

Reprinted from Teutsch et al[103] with permission from Macmillan Publishers Ltd: The evaluation of genomic applications in practice and prevention (EGAPP) initiative: methods of the EGAPP working group. *Genet Med.* 11(1):3-14, copyright 2009.

[a] Level 1 studies include systematic reviews of Level 2 studies, Level 2 studies include randomized clinical trials (RCT) of good quality, Level 3 studies include RCTs of poor quality, comparative studies with concurrent controls, and comparative study without concurrent controls. Level 4 studies include case series with either post-test or pre-test/post-test outcomes.
[b] Based on number of possible response categories and required confidence in results.
[c] Consistency can be assessed formally by testing for homogeneity, or, when data are limited, less formally using central estimates and range of values.
[d] Generalizability is the extension of findings and conclusions from one study to other settings.

Supplemental Table 11: Grades for Strength of Recommendations

Designation	Recommendation	Rationale
Strong Recommendation	Recommend For or Against a particular bone marrow synoptic reporting practice (Can include must or should)	Supported by convincing (high) or adequate (intermediate) quality of evidence and clear benefit that outweighs any harms
Recommendation	Recommend For or Against a particular bone marrow synoptic reporting practice (Can include should or may)	Some limitations in quality of evidence (adequate [intermediate]), balance of benefits and harms, values, or costs but panel concludes

		that there is sufficient evidence to inform a recommendation
Expert Consensus Opinion	Recommend For or Against a particular bone marrow synoptic reporting practice (Can include should or may)	Serious limitations in quality of evidence (inadequate [low] or insufficient), balance of benefits and harms, values or costs, but panel consensus is that a statement is necessary
No Recommendation	No Recommendation For or Against a particular bone marrow synoptic reporting practice	Insufficient evidence to provide a recommendation, balance of benefits and harms, values or costs

Supplemental Table 12. Summary of Studies for Statement 1

Element with significant outcome difference	Relevant disease or diagnosis	Number of studies reporting significant differences	Study	Outcome	Synoptic report (%)	Nonsynoptic report (%)	*P*-value
Completeness of required data elements	Prostate cancer, colorectal cancer, breast cancer, pancreatic cancer, thyroid cancer, melanoma	11	Aumann et al, 2012[57]	Reporting of required data elements	97.2	2.7-43.5	*P*<.001
			Austin et al, 2009[58]	Reporting of required data elements	88	27	*P*<.001
			Beattie et al, 2003[61]	Reporting of required data elements	73-100	21-87	*P*<.01
			Branston et al, 2002[6]	Reporting of required data elements	67.6-81.4	40.7-53.4	*P*<.001
			Gill et al, 2009[71]	Reporting of required data elements	84-100	11-66	*P*<.001
			Harvey et al, 2005[72]	Reporting of required data elements	4.1-70.9	0.2-3.7	*P*<.001
			Haugland et al, 2011[74]	Reporting of 11 required data elements	Not Reported (NR)	NR	*P*<.05 in favor of synoptic reports
			Karim et al, 2008[76]	Reporting of required data elements	94.8-100	38.7-97.3	*P*<.001
			Chan et al, 2008[62]	Reporting of required data elements, pre-synoptic versus post-synoptic	64-94	14-22	*P*<.001
			Idowu et al, 2010[75]	Reporting of required data elements	88	34	*P*=.01
			Messenger et al, 2011[91]	Reporting of required data elements	83-100	13.1-100	*P*<.001 in 6 of 10 required elements

Supplemental Table 13. Summary of Studies for Statement 2

Element with Significant Outcome Difference	Relevant Disease or Diagnosis	Number of Studies Reporting Significant Differences	Study	Results Summary	Comparison Favors/Shows Benefit/Difference for (Outcome)	*P*-value
White blood cells (WBC)	Ph+ acute lymphoblastic leukemia (ALL), P.vera	1	Gandemer et al, 2009[64]	Peripheral blood WBC<100K and bone marrow blast <5% on day 21 (low risk) was associated with significantly better event free and overall survival in Ph+ pediatric ALL	Event free survival: 55% low risk, 18% high risk; Overall survival: 79% low risk, 27% high risk	*P*=.002 (EFS) *P*=.003 (OS)
Hemoglobin (Hgb)	myelodysplasia, aplastic anemia	2	Kao et al, 2008[88]	Hgb level has additive prognostic value in myelodysplasic syndrome (MDS) for Intermediate 1-risk (Int-1), Intermediate – risk (Int-2) categories	Hgb>10g/dL is associated with better overall survival in Int-1 and Int-2 MDS	*P*<.001
			Greenberg et al, 2012[87]	In MDS significantly different survival and evolution to acute myeloid leukemia (AML) was associated with hemoglobin <10g	In MDS significantly different survival and evolution to AML was associated with hemoglobin <10g, platelet (plt) <100,000, absolute neutrophil count <0.08	*P*<.001
plt	myelodysplasia, myeloproliferative disease, adult T-cell leukemia/lymphoma	5	List et al, 2006[10]	Plt count <100,000 at baseline significantly associated with reduced probability of transfusion independence and cytogenetic response in lenalidomide treatment in MDS with 5q31 deletion	Thrombocytopenia <100,000 at baseline was associated with 39% transfusion independence versus 73% without thrombocytopenia; odds ratio for decreased cytogenetic response with versus without thrombocytopenia was 4.78	*P*=.001 transfusion independence *P*=.02 cytogenetic response
			Kao et	Plt count <100,000 was significantly	Plt >100,000 was	Chi^2 3.6

			al, 2008[88]	associated with International Prognostic Scoring System (IPSS) categories, overall survival and AML evolution in MDS patients	associated with 63% overall year median survival versus 5% <20,000	versus 1.4
			Kvasnicka et al, 2006[67]	Plt counts have prognostic impact in idiopathic myelofibrosis	Plt counts have prognostic impact in idiopathic myelofibrosis	Not given, references cited
			Wang et al, 2011[54]	Peripheral blood parameters plt, mean corpuscular volume (MCV), reticulocyte count, percent lymphocytes, are significantly different in severe aplastic anemia versus hypoplastic MDS in adult patients	Plt count, MCV, reticulocyte counts and percent lymphocytes were significantly different between severe aplastic anemia and hypoplastic MDS	*P*<.01
			Greenberg et al, 2012[87]	In MDS significantly different survival and evolution to AML was associated with plt <100,000	In MDS significantly different survival and evolution to AML was associated plt <100,000,	*P*<.001
Absolute neutrophil count	myelodsyplasia	2	Kao et al, 2008[88]	Absolute neutrophil count >1,500 was significantly associated IPSS categories, overall survival and AML evolution in MDS patients	Absolute neutrophil count >1,500 had 62% median overall survival versus 6% year median overall survival	Chi^2 3.9 versus 0.9
			Greenberg et al, 2012[87]	In MDS significantly different survival and evolution to AML was associated with absolute neutrophil count <0.8	In MDS significantly different survival and evolution to AML was associated with absolute neutrophil count <.8	*P*<.001
Reticulocyte count	aplastic anemia	1	Wang et al, 2011[54]	Reticulocyte count is significantly different in severe aplastic anemia (SAA) as compared to non-severe aplastic anemia (NSAA) and MDS	Mean reticulocyte count SAA 13.5 versus NSAA 35.7, MDS 55.5 x10E9/L	*P*<.01
Red cell Distribution Width (RDW)	aplastic anemia, MDS	1	Wang et al, 2011[54]	RDW is significantly different in severe and non-severe aplastic anemia versus hypoplastic MDS	Mean RDW 16.8% SAA, 17.4% NSSA, versus 20.4% MDS	*P*<.05

Supplemental Table 14. Summary of Studies for Statement 3

Element with Significant Outcome Difference	Relevant Disease or Diagnosis	Number of Studies Reporting Significant Differences	RefID	Results Summary	Comparison Favors/Shows Benefit/Difference for (Outcome)	*P*-value
Percent blast	Acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), myelodysplastic syndrome (MDS), myeloproliferative syndrome (MPN), aplastic anemia (AA)	7	Basso et al, 2009[15]	Residual disease of bone marrow (BM) blasts in day 15 childhood ALL is predictive of relapse	BM blasts <0.1%, 0.1<10%, >=10% measured by flow cytometry were associated with 5 year cumulative relapse in 7.5%, 17.5% and 47.2% respectively	*P*<.001
			Gandemer et al, 2009[64]	BM blast percent at day 21 is associated with prognosis	95% complete remission (CR) ≤ 5% blasts; 75% CR >5% blasts	*P*<.001
			Jabbour et al, 2006[24]	Marrow involvement in T-cell acute lymphoblastic leukemia (T-ALL) associated with overall survival; CR defined as ≤ 5% blasts	Overall survival (OS) BM positive 85%; OS BM negative 37%	*P*=.01
			Kao et al, 2008[88]	Uses International Prognostic Scoring System (IPSS) cytogenetic group blast percent definitions	Significant correlation with blast percent and cytopenias	*P*<.001
			Lugli et al, 2005[68]	BM blast percent is morphologic indicator of response in chronic myeloid leukemia (CML)	BM blast percent associated with cytogenetic response	*P*=.001
			Rowe et al, 2010[50]	BM blast percent as response criterion, residual disease post induction portends worse prognosis, but similar long term outcome with 1 or 2 cycles to CR	Various, including >10% blasts day 16 CR 54%; <10% blasts day 16 CR 84%	Not given, referenced cited
			Wang et al, 2011[54]	CD34+ blasts lower in AA than hypocellular MDS	Severe aplastic anemia (SAA) 0, non-severe aplastic anemia (NSAA)	*P*<.05

					0.12, MDS 2.2	
Dyspoiesis	MDS, MDS/MPN	5	Baumann et al, 2012[60]	Morphologic criteria can distinguish Refractory Cytopenia of Childhood versus severe aplastic anemia with high interobserver reliability	Patchy erythropoiesis with defective maturation and micromegakaryocytes were the most significant discriminators (no statistical values provided)	Kappa index 0.79 indicates substantial interobserver agreement
			Lugli et al, 2005[68]	Decrease of abnormal megakaryocytes correlates with cytogenetic response of CML on Imatinib treatment	Reduction of abnormal megakaryocytes to < or =10% significantly correlates with cytogenetic response	*P*<.001
			Wang et al, 2011[54]	Dyserythropoiesis is a key finding in MDS in distinction to severe aplastic anemia	Erythorpoietic pathological haemogenesis in 0% of severe aplastic anemia versus 95.5% of MDS	Not given
			Liu et al, 2009[90]	Incidence of specific dysplasia for granulocyte and megakaryocyte lineage was significantly different for abnormal karyotype MDS versus normal karyotype MDS or non-MDS cytopenias	Incidence of specific dysplasia for granulocyte and megakaryocyte lineage was significantly different for abnormal karyotype MDS versus normal karyotype MDS or non-MDS cytopenias	*P*<.05
			Thiele et al, 2011[95]	Morphologic bone marrow features distinguish essential thromocythemia versus early primary myelofibrosis	Megakaryocyte morphologic features, increased granulopoiesis and erythropoiesis can distinguish essential thrombocythemia versus primary myelofibrosis with high interobserver concordance	Concordance kappa 0.739 (*P*< .001), 95% confidence interval (CI) (0.651-0.827)

Percent lymphocytes, morphology	Non-Hodgkin Lymphoma (NHL), chronic lymphocytic leukemia (CLL)	2	Lombardo et al, 2002[27]	Response rate and relapse free survival (RFS) in follicular lymphoma treated with bleomycin, epidoxorubicin, cyclophosphamide, vincristine and prednisone (BACOP) was significantly different in patients with bone marrow involvement	Response rate and RFS in follicular lymphoma treated with BACOP was significantly worse in patients with bone marrow involvement	Response rate difference *P*<.001 RFS *P*<.001
			Musolino et al, 2010[92]	BM aspirate staging correlates with BM biopsy but has a sensitivity, specificity, negative and positive predictive value when compared with bone marrow biopsy	BM aspirate staging significantly correlates with BM biopsy results; BM aspirate positive predictive value (PPV) is 82% and negative predictive value (NPP) is 85% in indolent NHL versus 29% PPV and 89% NPP in aggressive NHL	*P*<.001 for correlation of BM aspirate and biopsy
Percent plasma cells	Plasma cell myeloma	1	Fernandez de Larrea et al, 2011[29]	BM plasma cells >1.5% after autologous transplantation had an increased risk of progression	BM plasma cells >1.5% after autologous transplantation had an increased risk of progression	*P*=.02

Supplemental Table 15. Summary of Studies for Statement 4

Element with Significant Outcome Difference	Relevant Disease or Diagnosis	Number of Studies Reporting Significant Differences	RefID	Results Summary	Comparison Favors/Shows Benefit/Difference for (Outcome)	*P*-value
Fibrosis	Myeloproliferative neoplasms (MPN), myelodysplastic syndrome (MDS)	6	Barbui et al, 2012[59]	Fibrosis at diagnosis in polycythemia vera (P.vera) significantly associated with splenomegaly, decreased thrombosis, post-polycythemic myelofibrosis	Palpable splenomegaly, thrombosis 1.1 versus 2.7 per 100 patient years, post-polycythemic myelofibrosis 2.2 versus 0.8 per 100 patient years	*P*=.03 (palpable splenomegaly) *P*=.01 (post-polycythemic myelofibrosis)
			Campbell et al, 2009[20]	Elevated reticulin fibrosis at presentation of essential thrombocythemia predicted higher rates of arterial thrombosis, major hemorrhage and myelofibrotic transformation	Arterial thrombosis hazard ratio (HR) 1.8, 95% confidence interval (CI), 1.1 to 2.9; major hemorrhage HR, 2.0; 95% CI, 1.0 to 3.9; myelofibrotic transformation HR, 5.5; 95% CI, 1.7 to 18.4;	*P*=.001 to *P*=.05
			Hultdin et al, 2007[8]	After 2 years of anagrelide therapy the reticulin and hyaluronan (HYA) scores were significantly higher than before treatment; indicating progression of disease	Reticulin and HYA scores were significantly higher than before treatment	*P*=.02 (reticulin score) *P=.002 (HYA score)*
			Kvasnicka et al, 2006[67]	Included ≥grade 2 fibrosis or cases with increase of 1 grade in <12 month follow-up; Survival rates in idiopathic myelofibrosis (IMF): Prefibrotic and early-fibrotic stages of IMF display significantly higher 5 and 10 years relative survival rates than advanced (classical) stages with prominent myelofibrosis (IMF-2/3 or myeloid metaplasia).	Essential thrombocythemia (ET) has better survival than prefibrotic and early IMF (IMF0, IMF-1)	*P*<.001

				Myelofibrosis Survival rates in polycythemia rubra vera: 10 to 20% of patients present with mild to moderate reticulin fibrosis at onset; development of marked collagen myelofibrosis occurred in less than 20% of patients and displayed strong time-related progression		
			Lugli et al, 2005[68]	Reduction of fibrosis significantly associated with cytogenetic response	Fibrosis ≤ grade 2 is associated with higher rate of complete or other cytogenetic response	*P*=.01
			Green berg et al, 2012[87]	Significantly different survival and evolution to acute myeloid leukemia (AML) were associated (p<0.001) with marrow fibrosis	Patients with associated with bone marrow (BM) fibrosis had poorer survival and higher incidence of transformation to AML than those who did not have associated bone marrow fibrosis	*P*<.001
Cellularity	MPN, aplastic anemia, MPD	3	Wang et al, 2011[54]	Cellularity of <20-30% is defining hypoplastic MDS	Hypoplastic MDS requires BM biopsy cellularity <30% age <60 years, <20% age ≥60years	*P*<.05
			Thiele et al, 2011[95]	Cellularity determination can help, in addition to other morphologic features, to distinguish between ET and early, pre-fibrotic primary myelofibrosis (PMF).	Normal or slightly increased cellularity present in ET is significantly different from marked increase in age-matched cellularity in early pre-fibrotic stage of PMF with high diagnostic concordance of 74%	*P*<.001
			Lugli et al, 2005[68]	Normalization of cellularity was significantly associated with cytogenetic response in chronic myeloid leukemia (CML) on imatinib treatment	Age adjusted normal cellularity was significantly associated with complete or other cytogenetic response	*P*=.001

Cellularity/Involvement by lymphoma	Non-Hodgkin and Hodgkin Lymphoma	3	Lombardo et al, 2002[27]	BM involvement by follicular lymphoma is significantly associated with adverse response rate and relapse free survival (RFS)	BM involvement by follicular lymphoma is significantly associated with adverse response rate and RFS	*P*<.01 response rate, *P*<.04 RFS
			Gallamini et al, 2004[63]	Bone marrow involvement by peripheral T-cell lymphoma is associated with poorer outcome (increased relative risk of 1.454, CI 95%, *P*=.03) in multivariate analysis and worse overall survival in univariate analysis (*P*<.001)	Bone marrow involvement by peripheral T-cell lymphoma is associated with worse outcome after therapy and worse overall survival	*P*=.03 *P*<.001
			Takasaki et al, 2007[51]	Bone marrow involvement is strongly associated with adverse outcome in adult T-cell leukemia/lymphoma (ATLL) (HR1.9)	Presence of bone marrow involvement in ATLL is associated with increased risk of death when compared to patients with no marrow involvement	*P*=.001
Blast %	AML	1	Rowe et al, 2010[50]	BM blast % as response criterion for AML, residual disease post induction portends worse prognosis, but similar long term survival if complete remission is achieved with 2 cycles of induction chemotherapy	There was a significant improvement of complete remission if patients with residual leukemia after first induction received a second induction chemotherapy	*P*<.001

Supplemental Table 16. Summary of Studies for Statement 5

Element with significant outcome difference	Relevant disease or diagnosis	Number of studies reporting significant differences	Study	Results summary	Comparison favors/shows benefit/difference for (outcome)	*P*-value
Flow cytometry	Acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), myelodysplastic syndrome (MDS), Lymphoma, chronic lymphocytic leukemia (CLL)	8	Bjorklund et al, 2009[18]	High concordance of reported minimum residual disease (MRD) levels by flow among laboratories at two different cut-off levels	Substantial agreement at cut-off level .1% concordance 91.6% with kappa 0.8234, at cut-off level .01%, concordance 85.3% with kappa 0.6859	*P*<.001 *P*<.001
			Bottcher et al, 2008[19]	Flow cytometry of bone marrow and/or peripheral blood is more sensitive than bone marrow (BM) histology in 9.4% of patients with mantle cell lymphoma	BM involvement detected by flow cytometry only was significantly lower in bone marrows with negative BM histology	*P*<.001
			Langebrake et al, 2006[25]	Correlation of 3-year event free survival (EFS) with negative bone marrow was highest on day 15 Bone Marrow Puncture 1 (BMP1) at significance level *P*=.03, and day 21-28 (BMP2) at *P*=.03	Residual disease monitored with flow cytometry before second induction is predictive of 3-year EFS	*P*=.03 *P*=.03
			Irving et al, 2009[9]	Concordance at MRD level above or below .01% level was 86%, no statistical analysis	MRD levels at different laboratories	Not given
			Moreton et al, 2005[35]	Patients with MRD-negative complete remission (CR) had longer treatment free and overall survival than MRD-positive CR	Minimal residual disease detection with flow cytometry	*P*<.001
			Morgado et al, 2012[36]	Although the authors claim that CD25 is the better, more efficient marker, the p values for comparison are not significant at *P*=.40 to *P*=.85 in the statistical analysis	Aberrant expression of CD25 and/or CD2 in mast cells	*P*-value is not significant
			Perea et al, 2005[37]	CD2 and CD36 expression are significantly associated with a lower overall survival and adverse karyotype	Immunophenotype by flow cytometry, expression of CD2, C36	*P*=.04 (CD2) *P*=.03 (CD36)

			Chopra et al, 2012[43]	Flow cytometric expression patterns (mean fluorescence intensity [MFI] and % positive cells) are significantly different in MDS versus normal controls	MFI for CD71 on erythroid cells and for CD38 on CD34+ positive cells, and % CD15+CD34+ positive cells are statistically different in proven and suspected MDS versus normal and non-MDS control marrows	*P*=.02 (CD71) *P*=.01 (CD38 on $CD34^{+}$) *P*=.05 (CD15+CD34+)
Cytogenetics (chromosomal analysis)	AML, MDS, ALL	3	Chen et al, 2011[21]	Relapse free survival (RFS), overall survival (OS) are significantly worse in patients with cytogenetic abnormalities versus no abnormalities after achieving CR post induction chemotherapy, regardless of initial cytogenetic risk group	Persistent cytogenetic abnormalities after induction chemotherapy for AML were an independent predictor for RFS *P*<.001 and OS *P*=.001; patients with and without stem cell transplant showed a trend for better RFS *P*=.08 but not OS *P*=.25 and OS in the Stem-cell Transplantation group	*P*<.001
			Kern et al, 2003[31]	Intermediate and unfavorable cytogenetics is associated with worse OS, EFS and RFS in AML	OS, EFS, and RFS in patients with acute myeloid leukemia are significantly worse in patients with intermediate/unfavorable cytogenetics at diagnosis	*P*<.001 - *P*=.04
			Vance et al, 2007[53]	Cytogenetic risk categories in diagnosis of AML; fluorescent in situ hybridization (FISH) analysis, cytogenetic analysis	Concordance rate of FISH and cytogenetic 98-100%	*P*<.001
FISH		1	Vance et al, 2007[53]	cytogenetic risk categories in diagnosis of AML; FISH analysis, cytogenetic analysis	Concordance rate of FISH and cytogenetic 98-100%	*P*<.001
Immunohistochemistry	CLL	1	Schlette et al, 2009[28]	p53-IHC was significantly associated with lower CR, lower partial remission (PR), no response to therapy, lower 5-year survival independent of ZAP70 and IgVH hypermutation	CR, PR, no response to therapy, 5-year OS	*P*<.001 (CR) *P*=.05 (PR) *P*<.001 (no response to therapy)

						P<.001 (5-year OS)
Bone marrow isolated tumor cell detection (ITC)	Breast cancer	2	Wiedswang et al, 2003[55]	isolated tumor cell (ITC)-positive patients had a higher risk of systemic relapse and death	Patients with ITCs identified by immunohistochemistry or other methods had poorer survival (distant disease-free survival and breast-cancer-specific survival) than those patients where tumor cells were not identified in the marrow	*P*<.001
			Janni et al, 2012[100]	Patients without ITC had significantly longer survival than ITC-positive patients	Identification of ITC had worse overall survival (103.3 months) compared to patients without detected ITC (165.6 months)	*P*<.001
Molecular analysis	AML, CLL, chronic myeloid leukemia (CML), lymphoma	6	Martinelli et al, 2006[11]	bcr-abl transcript levels in bone marrow and peripheral blood of CML patients correlate with cytogenetic response to imatinib therapy	Molecular transcript levels are significantly related to cytogenetic response; at 12 months therapy significant difference of transcript levels in BM versus PB *P*<.01, at 18-24 months no significant detectable difference	*P*<.001 for BM, *P*<.01 for PB
			Merx et al, 2002[34]	Ratio of bcr-abl/abl transcripts in peripheral blood by real time polymerase chain reaction (RT-PCR) and cytogenetic response	bcr-abl/abl ratios by RT-PCR on peripheral blood after two months of imatinib therapy correlated with major cytogenetic response at 6 months	*P*<.001
			Quintas-Cardama et al, 2009[38]	Response, bcr-abl/abl ratio by polymerase chain reaction (PCR)	Cytogenetic response or major molecular response is significantly different at 3 months *P*<.001 and at 6 months *P*<.001 but not at 12 months and correlates with RT-PCR (no statistical	*P*<.001

					value given)	
			Lane et al, 2008[80]	≥1 log rise in real time quantitative PCR (RQ-PCR) transcript levels defines molecular relapse in core binding factor (CBF) AML and predicts subsequent morphologic relapse; RQ-PCR levels at diagnosis, post-induction chemotherapy and post-consolidation were not predictive of outcome.	1 $\log_{10}$ increase in RQ-PCR hazard leukemia free survival (LFS) 8.6 95% Confidence Interval (CI): 1.8 – 42	*P*=.01
			Liu et al, 2012[26]	Immunoglobulin Heavy (IGH) and/or BCL1/JH RQ-PCR for minimal residual disease in peripheral blood (PB) after induction chemotherapy is an independent predictor of progression free survival (time to progression) and differs from BM MRD	Sustained molecular response	*P*=.02 for PB
			Lundan et al, 2008[32]	PCR for residual disease in CML highly correlates with complete cytogenetic response by metaphase FISH and should be reported according to International Scale	Major molecular response according to the International Scale in BCR-ABL/GUS transcript levels corresponded to a ratio of .035% (PB) and .034%	*P*<.001 correlation of BM and PB RQ-PCR with FISH

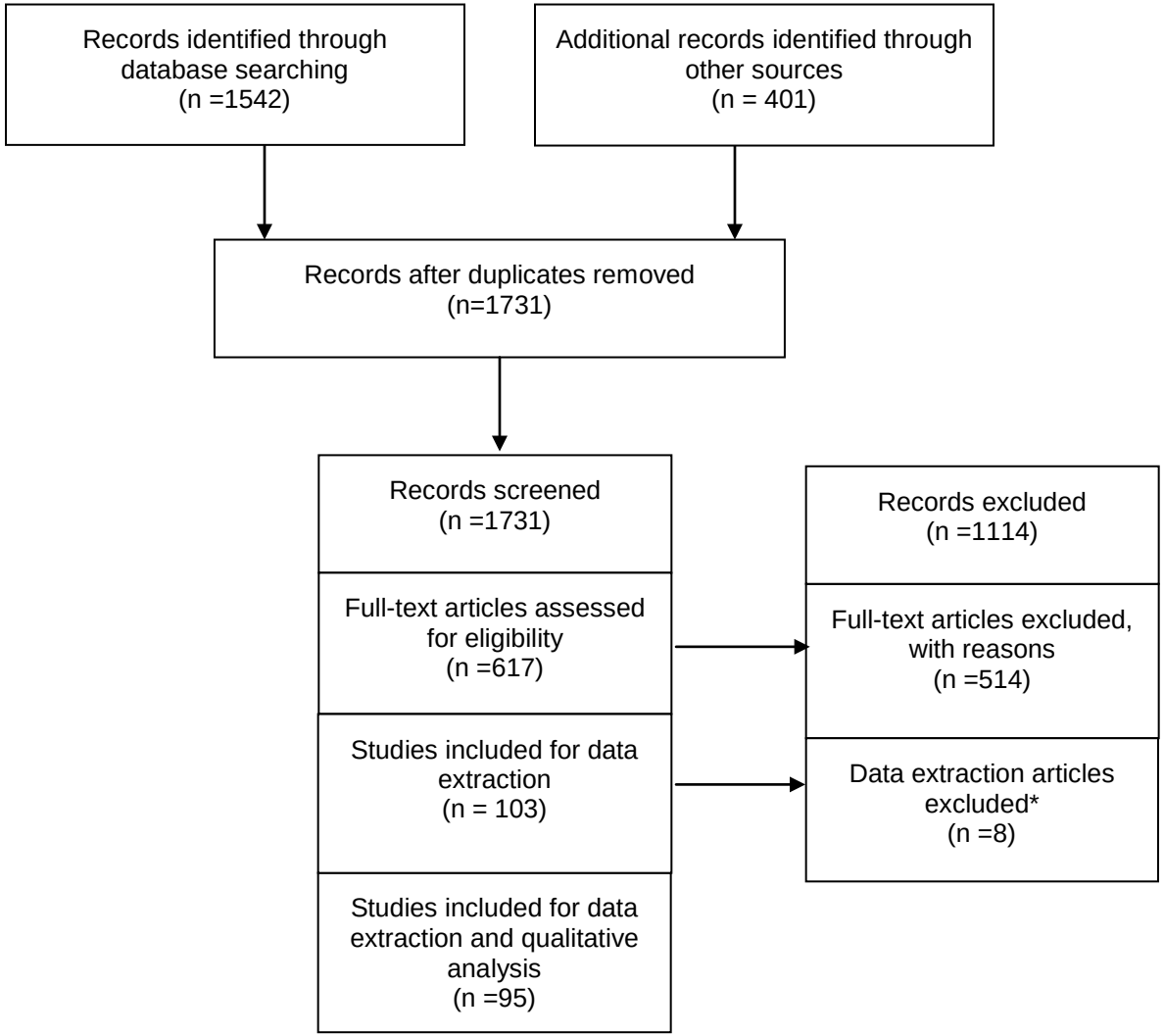
Supplemental Table 17. Summary of Studies for Statement 9

Element with significant outcome difference	Relevant disease or diagnosis	Number of studies reporting significant differences	Study	Results summary	Comparison favors/shows benefit/difference for (outcome)	*P*-value
Age	Acute lymphoblastic leukemia (ALL), myeloproliferative disorders essential thrombocythemia (ET), polycythemia rubra vera (PV), idiopathic myelofibrosis (IMF), peripheral T-cell lymphoma	3	Gandemer et al, 2009[64]	Age is an important prognostic factor in children with ALL	Children <10 years old had more favorable 5 year-event free (48% versus 15%) and 5-year overall survival (61% versus 23%)	*P*=.01 (EFS and OS)
			Kvasnicka et al, 2006[67]	Patients >60 years old had a significantly higher disease specific loss in life expectancy	Patients >60 years old had a significantly higher disease specific loss in life expectancy	*P*=.003
			Gallamini et al, 2004[63]	Patients >60 years old had worse overall survival (OS)	Patients >60 years old had worse OS	*P*=.002
Performance status	Peripheral T-cell lymphoma, Hypoplastic myelodysplastic syndromes	2	Gallamini et al, 2004[63]	Eastern Cooperative Oncology Group (ECOG) performance status 2 or higher was associated with worse survival	ECOG performance status 2 or higher was associated with worse survival	*P*<.001
			Garcia-Manero et al, 2012[101]	Performance status 2 or higher was an adverse prognostic factor	Performance status 2 or higher was an adverse prognostic factor	*P*=.005
Lactate dehydrogenase (LDH)	Acute myeloid leukemia (AML), Peripheral T-cell lymphoma, primary bone marrow (BM) Non-Hodgkin lymphoma (NHL), Hypoplastic MDS	4	Gallamini et al, 2004[63]	LDH value more than 1x normal is associated with worse survival	LDH value more than 1x normal is associated with worse survival	*P*<.001
			Czuczman et al, 2006[7]	LDH correlates significantly with time to progression and duration of response in NHL	Patients with low or normal LDH had 16.6 months to progression versus 11.5; duration of response 14.5 versus 7.9 months	*P*=.01 *P*=.01
			Garcia-Manero et	LDH >600IU/L was and adverse prognostic factor	LDH >600IU/L was and adverse prognostic	*P*=.01

			al, 2012[101]		factor	
			Kern et al, 2003[31]	LDH was significantly associated with complete remission (CR), event-free survival (EFS), relapse-free survival (RFS) and overall survival (OS) in patients with AML	LDH was significantly associated with CR *P*=.007, EFS *P*<.001, RFS *P*<.001 and OS *P*.004 in patients with AML	*P*=.004 to *P*<.001
Staging	Non-Hodgkin Lymphoma, peripheral T-cell lymphoma	2	Lombardo et al, 2002[27]	Low stage was significantly associated with better response rate, RFS and OS	Stage 1-2: 70.3%,Stage 3-4 44.8% RFS; Stage 1-2: 95.6%,Stage 3-4 85.1% OS;	RFS *P*=.04 OS *P*=.01
			Gallamini et al, 2004[63]	Stage 3 or higher was associated with worse survival	Stage 3 or higher was associated with worse survival	*P*<.001
Prognostic scoring system	Non-Hodgkin Lymphoma, peripheral T-cell lymphoma	2	Lombardo et al, 2002[27]	Low international prognostic index (IPI) score, Italian Lymphoma Intergroup (ILI) score were significantly associated with superior overall survival	Overall 5 year survival IPI 0-1: 94.4% ILI 0-2 89.5% versus IPI 2-3: 87.5%, ILI 3-4: 57.1%	*P*=.03 IPI score and ILI score
			Gallamini et al, 2004[63]	IPI score was significantly associated with survival		*P*<.001
Peripheral blood parameters	See recommendation 3 peripheral blood	6	List et al, 2006,[10] Gandemer et al, 2009,[64] Kao et al, 2008,[88] Kvasnicka et al, 2006,[67] Wang et al, 2011,[54] Greenberg	See recommendation 3 peripheral blood		

			et al, 2012[87]			

Supplemental Figure 1: Literature Review Flow Diagram



*Excluded based on expert opinion, did not meet minimum quality standards, presented incomplete data or data that were not in useable formats
**Adapted from Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med.*2009;6:e1000097.[104]

Supplemental Figure 2: Bone Marrow Synoptic Reporting Ovid Search Strings

Ovid Search #1

1. *Bone Marrow/pa
2. *Bone Marrow Examination/
3. *Bone Marrow Cells/pa
4. ("bone marrow" or hematopoetic or "trephine biops$").ab. /freq=2
5. or/1-4
6. Multiple Myeloma/di, pa
7. exp Amyloidosis/di, pa
8. Leukemia, Myeloid, Acute/di, pa
9. Precursor Cell Lymphoblastic Leukemia-Lymphoma/di, pa
10. Leukemia, Myelogenous, Chronic, BCR-ABL Positive/di, pa
11. Primary Myelofibrosis/di, pa
12. Polycythemia Vera/di, pa
13. Thrombocythemia, Essential/di, pa
14. Myelodysplastic Syndromes/di, pa
15. Myelodysplastic-Myeloproliferative Diseases/di, pa
16. exp Anemia, Aplastic/di, pa
17. exp Myeloproliferative Disorders/di, pa
18. Hodgkin Disease/di, pa
19. exp Lymphoma, Non-Hodgkin/di, pa
20. Leukemia, Lymphocytic, Chronic, B-Cell/di, pa
21. exp Anemia/di, pa
22. Parvovirus B19, Human/
23. Anemia, Iron-Deficiency/di, pa
24. Vitamin B 12 Deficiency/di, pa
25. Folic Acid Deficiency/di, pa
26. Osteitis Deformans/di, pa
27. Purpura, Thrombocytopenic, Idiopathic/di, pa
28. chronic myeloproliferative neoplasm$.ab. /freq=2
29. chronic myeloproliferative dis$.ab. /freq=2
30. (iron stor$ or myeloma or am?emia).ab. /freq=2
31. idiopathic thrombocytopenic purpura.ab. /freq=2
32. bone marrow failure.ab. /freq=2
33. paget's disease of the bone.ab. /freq=2
34. folate deficien$.ab. /freq=2
35. parvovirus b19.ab. /freq=2
36. idiopathic immune thrombocytopenia.ab. /freq=2
37. or/6-36
38. 5 and 37
39. Meta-Analysis as Topic/
40. meta analysis.pt.
41. meta?analy$.tw.
42. (pooled analy$ or statistical pooling or mathematical pooling or statistical summar$ or mathematical summar$ or quantitative synthes?s or quantitative overview).tw.
43. (systematic adj (review$ or overview?)).tw.
44. (exp Review Literature as topic/ or review.pt. or exp review/) and systematic.tw.
45. or/39-44
46. (selection criteria or data extraction or quality assessment or jadad scale or methodological quality).ab.
47. (study adj selection).ab.
48. 46 or 47
49. exp randomized controlled trials as topic/ or exp clinical trials, phase III as topic/ or exp clinical trials, phase IV as topic/
50. (randomized controlled trial or clinical trial, phase?III or clinical trial, phase?IV).pt.

51. random allocation/ or double blind method/ or single blind method/
52. (randomi$ control$ trial? or rct or phase?I or phase?II or phase?III or phase?IV or phase?1 or phase?2 or phase?3 or phase?4).tw.
53. or/49-52
54. exp clinical trial/ or exp clinical trial as topic/
55. (clinical trial or clinical trial, phase II or controlled clinical trial).pt.
56. 54 or 55
57. ((singl$ or doubl$ or treb$ or tripl$) adj3 (blind$ or mask$ or dummy)).tw.
58. (allocated adj3 random).tw.
59. (clinic$ adj3 trial$1).tw.
60. ((experimental or study or research) adj3 design).tw.
61. or/57-60
62. *practice guidelines/
63. (practice adj3 guideline?).tw.
64. practice guideline.pt.
65. or/62-64
66. comparative study.pt.
67. consensus development conference.pt.
68. consensus development conference, nih.pt.
69. evaluation studies.pt.
70. or/66-69
71. research support, nih, extramural.pt.
72. research support, nih, intramural.pt.
73. research support, non us gov't.pt.
74. research support, us gov't, non phs.pt.
75. research support, us gov't, phs.pt.
76. or/71-75
77. 45 or 48 or 53 or 56 or 61 or 65 or 70 or 76
78. (comment or interview or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case report or historical article).pt.
79. 77 not 78
80. 38 and 79
81. Limit 80 to (English language and humans and yr="2002-2012")
82. bone marrow.ab./freq=3
83. 80 and 81

Ovid Search #2

1. *Bone Marrow/pa
2. *Bone Marrow Examination/
3. *Bone Marrow Cells/pa
4. ("bone marrow" or hematopoetic or "trephine biops$").ab. /freq=2
5. or/1-4
6. *Histocytological Preparation Techniques/
7. *"Staining and Labeling"/
8. *"Silver Staining"/
9. *Histocytochemistry/
10. exp *Immunohistochemistry/
11. *Flow Cytometry/
12. *Cytogenetics/
13. *"In situ hybridization, fluorescence"/
14. exp *molecular diagnostic techniques/
15. *reticulin/
16. *congo red/
17. ancillary.ab. /freq=2
18. "flow cytometry".ab. /freq=2
19. cytogenetic$.ab. /freq=2

20. "cell count$".ab. /freq=2
21. immunohistochem$.ab. /freq=2
22. "DNA sequenc$".ab. /freq=2
23. "molecular stain$".ab. /freq=2
24. "molecular diagn$".ab. /freq=2
25. immunophenotype$.ab. /freq=2
26. clonality.ab. /freq=2
27. 27 "in situ hybridization".ab. /freq=2
28. FISH.ab. /freq=2
29. "special stain$".ab. /freq=2
30. reticulin.ab. /freq=2
31. "congo red".ab. /freq=2
32. "acid fast".ab. /freq=2
33. "AFB stain$".ab. /freq=2
34. "fungal stain$".ab. /freq=2
35. or/6-34
36. 5 and 35
37. Meta-Analysis as Topic/
38. meta analysis.pt.
39. meta?analy$.tw.
40. (pooled analy$ or statistical pooling or mathematical pooling or statistical summar$ or mathematical summar$ or quantitative synthes?s or quantitative overview).tw.
41. (systematic adj (review$ or overview?)).tw.
42. (exp Review Literature as topic/ or review.pt. or exp review/) and systematic.tw.
43. or/37-42
44. (selection criteria or data extraction or quality assessment or jadad scale or methodological quality).ab.
45. (study adj selection).ab.
46. 44 or 45
47. exp randomized controlled trials as topic/ or exp clinical trials, phase III as topic/ or exp clinical trials, phase IV as topic/
48. (randomized controlled trial or clinical trial, phase?III or clinical trial, phase?IV).pt.
49. random allocation/ or double blind method/ or single blind method/
50. (randomi$ control$ trial? or rct or phase?I or phase?II or phase?III or phase?IV or phase?1 or phase?2 or phase?3 or phase?4).tw.
51. or/47-50
52. exp clinical trial/ or exp clinical trial as topic/
53. (clinical trial or clinical trial, phase II or controlled clinical trial).pt.
54. 52 or 53
55. ((singl$ or doubl$ or treb$ or tripl$) adj3 (blind$ or mask$ or dummy)).tw.
56. (allocated adj3 random).tw.
57. (clinic$ adj3 trial$1).tw.
58. ((experimental or study or research) adj3 design).tw.
59. or/55-58
60. *practice guidelines/
61. (practice adj3 guideline?).tw.
62. practice guideline.pt.
63. or/60-62
64. comparative study.pt.
65. consensus development conference.pt.
66. consensus development conference, nih.pt.
67. evaluation studies.pt.
68. or/64-67
69. research support, nih, extramural.pt.
70. research support, nih, intramural.pt.
71. research support, non us gov't.pt.

72. research support, us gov't, non phs.pt.
73. research support, us gov't, phs.pt.
74. or/69-73
75. 43 or 46 or 51 or 54 or 59 or 63 or 68 or 74
76. (comment or interview or letter or editorial or note or erratum or short survey or news or newspaper article or patient education handout or case report or historical article).pt.
77. 75 not 76
78. 36 and 77
79. Limit 78 to (English language and humans and yr="2002-2012")
80. bone marrow.ab./freq=3
81. 79 and 80

OVID Search #3

1. Bone Marrow/
2. Bone Marrow Examination/
3. Bone Marrow Cells/
4. Pathology, Clinical/
5. Pathology, Surgical/
6. ("bone marrow" or hematopoetic or "trephine biops$").tw.
7. patholog$.ab. /freq=2
8. or/1-7
9. Clinical Laboratory information Systems/
10. Database Management Systems/
11. exp Medical Records Systems, Computerized/st
12. Medical Records/st
13. Practice guidelines as topic/
14. records as topic/
15. vocabulary, controlled/
16. terminology as topic/
17. clinical protocols/
18. databases as topic/
19. "evidence-based medicine"/
20. "forms and records control"/
21. "information management"/mt
22. laboratories/st
23. "medical informatics"/
24. "medical informatics applications"/
25. "natural language processing"/
26. "reproducibility of results"/
27. software/
28. user-computer interface/
29. systems integration/
30. "systematized nomenclature of medicine"/
31. "interdisciplinary communication"/
32. research design/
33. accreditation/
34. clinical protocols/
35. communication/
36. medical errors/
37. "pathology report$".tw.
38. "synoptic report$".tw.
39. (checklist$ or guideline$).ti.
40. data element$.tw.
41. (comprehension or "medical error$").tw.
42. "web based".tw.
43. or/1-34

44. report$.ab. /freq=2
45. 43 and 44
46. 8 and 45
47. limit 46 to (English language and humans and yr="2002-2012")

REFERENCES

1. National Comprehensive Cancer Network. NCCN Guidelines. National Comprehensive Cancer Network website. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed October 12, 2015.
2. Centers for Medicare & Medicaid Services. Physician Quality Reporting System. Centers for Medicare & Medicaid Services website. https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/PQRS/index.html?redirect=/pqri/. Updated June 12, 2015. Accessed October 12, 2015.
3. Verkerk K, Van Veenendaal H, Severens JL, Hendriks EJ, Burgers JS. Considered judgement in evidence-based guideline development. *Int J Qual Health Care*. 2006;18(5):365-369.
4. Institute of Medicine (IOM). *Clinical Practice Guidelines We Can Trust*. Washington, DC: National Academies Press; 2011.
5. Alvarnas JC, Brown PA, Aoun P, et al. Acute lymphoblastic leukemia. *J Natl Compr Canc Netw*. 2012;10(7):858-914.
6. Branston LK, Greening S, Newcombe RG, et al. The implementation of guidelines and computerised forms improves the completeness of cancer pathology reporting. The CROPS project: a randomised controlled trial in pathology. *Eur J Cancer*. 2002;38(6):764-772.
7. Czuczman MS, Grillo-Lopez AJ, Alkuzweny B, Weaver R, Larocca A, McLaughlin P. Prognostic factors for non-Hodgkin's lymphoma patients treated with chemotherapy may not predict outcome in patients treated with rituximab. *Leuk Lymphoma*. 2006;47(9):1830-1840.
8. Hultdin M, Sundstrom G, Wahlin A, et al. Progression of bone marrow fibrosis in patients with essential thrombocythemia and polycythemia vera during anagrelide treatment. *Med Oncol*. 2007;24(1):63-70.
9. Irving J, Jesson J, Virgo P, et al. Establishment and validation of a standard protocol for the detection of minimal residual disease in B lineage childhood acute lymphoblastic leukemia by flow cytometry in a multi-center setting. *Haematologica*. 2009;94(6):870-874.
10. List A, Dewald G, Bennett J, et al. Lenalidomide in the myelodysplastic syndrome with chromosome 5q deletion. *N Engl J Med*. 2006;355(14):1456-1465.
11. Martinelli G, Iacobucci I, Rosti G, et al. Prediction of response to imatinib by prospective quantitation of BCR-ABL transcript in late chronic phase chronic myeloid leukemia patients. *Ann Oncol*. 2006;17(3):495-502.
12. Powsner SM, Costa J, Homer RJ. Clinicians are from Mars and pathologists are from Venus. *Arch Pathol Lab Med*. 2000;124(7):1040-1046.
13. Valenstein PN. Formatting pathology reports: applying four design principles to improve communication and patient safety. *Arch Pathol Lab Med*. 2008;132(1):84-94.
14. Vandvik PO, Santesso N, Akl EA, et al. Formatting modifications in GRADE evidence profiles improved guideline panelists comprehension and accessibility to information. A randomized trial. *J Clin Epidemiol*. 2012;65(7):748-755.

15. Basso G, Veltroni M, Valsecchi MG, et al. Risk of relapse of childhood acute lymphoblastic leukemia is predicted by flow cytometric measurement of residual disease on day 15 bone marrow. *J Clin Oncol*. 2009;27(31):5168-5174.

16. Benoy IH, Elst H, Philips M, et al. Prognostic significance of disseminated tumor cells as detected by quantitative real-time reverse-transcriptase polymerase chain reaction in patients with breast cancer. *Clin Breast Cancer*. 2006;7(2):146-152.

17. Bessho M, Hotta T, Ohyashiki K, et al. Multicenter prospective study of clonal complications in adult aplastic anemia patients following recombinant human granulocyte colony-stimulating factor (lenograstim) administration. *Int J Hematol*. 2003;77(2):152-158.

18. Bjorklund E, Matinlauri I, Tierens A, et al. Quality control of flow cytometry data analysis for evaluation of minimal residual disease in bone marrow from acute leukemia patients during treatment. *J Pediatr Hematol Oncol*. 2009;31(6):406-415.

19. Bottcher S, Ritgen M, Buske S, et al. Minimal residual disease detection in mantle cell lymphoma: methods and significance of four-color flow cytometry compared to consensus IGH-polymerase chain reaction at initial staging and for follow-up examinations. *Haematologica*. 2008;93(4):551-559.

20. Campbell PJ, Bareford D, Erber WN, et al. Reticulin accumulation in essential thrombocythemia: prognostic significance and relationship to therapy. *J Clin Oncol*. 2009;27(18):2991-2999.

21. Chen Y, Cortes J, Estrov Z, et al. Persistence of cytogenetic abnormalities at complete remission after induction in patients with acute myeloid leukemia: prognostic significance and the potential role of allogeneic stem-cell transplantation. *J Clin Oncol*. 2011;29(18):2507-2513.

22. Cherry AM, Brockman SR, Paternoster SF, et al. Comparison of interphase FISH and metaphase cytogenetics to study myelodysplastic syndrome: an Eastern Cooperative Oncology Group (ECOG) study. *Leuk Res*. 2003;27(12):1085-1090.

23. Falini B, Mecucci C, Saglio G, et al. NPM1 mutations and cytoplasmic nucleophosmin are mutually exclusive of recurrent genetic abnormalities: a comparative analysis of 2562 patients with acute myeloid leukemia. *Haematologica*. 2008;93(3):439-442.

24. Jabbour E, Koscielny S, Sebban C, et al. High survival rate with the LMT-89 regimen in lymphoblastic lymphoma (LL), but not in T-cell acute lymphoblastic leukemia (T-ALL). *Leukemia*. 2006;20(5):814-819.

25. Langebrake C, Creutzig U, Dworzak M, et al. Residual disease monitoring in childhood acute myeloid leukemia by multiparameter flow cytometry: the MRD-AML-BFM Study Group. *J Clin Oncol*. 2006;24(22):3686-3692.

26. Liu H, Johnson JL, Koval G, et al. Detection of minimal residual disease following induction immunochemotherapy predicts progression free survival in mantle cell lymphoma: final results of CALGB 59909. *Haematologica*. 2012;97(4):579-585.

27. Lombardo M, Morabito F, Merli F, et al. Bleomycin, epidoxorubicin, cyclophosphamide, vincristine and prednisone (BACOP) in patients with follicular non-Hodgkin's lymphoma: results of a prospective, multicenter study of the Gruppo Italiano Per Lo Studio Dei Linfomi (GISL). *Leuk Lymphoma*. 2002;43(9):1795-1801.

28. Schlette EJ, Admirand J, Wierda W, et al. p53 expression by immunohistochemistry is an important determinant of survival in patients with chronic lymphocytic leukemia receiving frontline chemo-immunotherapy. *Leuk Lymphoma*. 2009;50(10):1597-1605.

29. Fernandez de Larrea C, Tovar N, Rozman M, et al. Multiple myeloma in serologic complete remission after autologous stem cell transplantation: impact of bone marrow plasma cell assessment by conventional morphology on disease progression. *Biol Blood Marrow Transplant*. 2011;17(7):1084-1087.

30. Haferlach T, Schoch C, Loffler H, et al. Morphologic dysplasia in de novo acute myeloid leukemia (AML) is related to unfavorable cytogenetics but has no independent prognostic relevance under the conditions of intensive induction therapy: results of a multiparameter analysis from the German AML Cooperative Group studies. *J Clin Oncol*. 2003;21(2):256-265.

31. Kern W, Haferlach T, Schoch C, et al. Early blast clearance by remission induction therapy is a major independent prognostic factor for both achievement of complete remission and long-term outcome in acute myeloid leukemia: data from the German AML Cooperative Group (AMLCG) 1992 Trial. *Blood*. 2003;101(1):64-70.

32. Lundan T, Juvonen V, Mueller MC, et al. Comparison of bone marrow high mitotic index metaphase fluorescence in situ hybridization to peripheral blood and bone marrow real time quantitative polymerase chain reaction on the International Scale for detecting residual disease in chronic myeloid leukemia. *Haematologica*. 2008;93(2):178-185.

33. Maynadie M, Picard F, Husson B, et al. Immunophenotypic clustering of myelodysplastic syndromes. *Blood*. 2002;100(7):2349-2356.

34. Merx K, Muller MC, Kreil S, et al. Early reduction of BCR-ABL mRNA transcript levels predicts cytogenetic response in chronic phase CML patients treated with imatinib after failure of interferon alpha. *Leukemia*. 2002;16(9):1579-1583.

35. Moreton P, Kennedy B, Lucas G, et al. Eradication of minimal residual disease in B-cell chronic lymphocytic leukemia after alemtuzumab therapy is associated with prolonged survival. *J Clin Oncol*. 2005;23(13):2971-2979.

36. Morgado JMT, Sanchez-Munoz L, Teodosio CG, et al. Immunophenotyping in systemic mastocytosis diagnosis: 'CD25 positive' alone is more informative than the 'CD25 and/or CD2' WHO criterion. *Mod Pathol*. 2012;25(4):516-521.

37. Perea G, Domingo A, Villamor N, et al. Adverse prognostic impact of CD36 and CD2 expression in adult de novo acute myeloid leukemia patients. *Leuk Res*. 2005;29(10):1109-1116.

38. Quintas-Cardama A, Kantarjian H, Jones D, et al. Delayed achievement of cytogenetic and molecular response is associated with increased risk of progression among patients with chronic myeloid leukemia in early chronic phase receiving high-dose or standard-dose imatinib therapy. *Blood*. 2009;113(25):6315-6321.

39. Ratei R, Basso G, Dworzak M, et al. Monitoring treatment response of childhood precursor B-cell acute lymphoblastic leukemia in the AIEOP-BFM-ALL 2000 protocol with multiparameter flow cytometry: predictive impact of early blast reduction on the remission status after induction. *Leukemia*. 2009;23(3):528-534.

40. Ribera J-M, Ortega J-J, Oriol A, et al. Prognostic value of karyotypic analysis in children and adults with high-risk acute lymphoblastic leukemia included in the PETHEMA ALL-93 trial. *Haematologica*. 2002;87(2):154-166.

41. Sievers EL, Lange BJ, Alonzo TA, et al. Immunophenotypic evidence of leukemia after induction therapy predicts relapse: results from a prospective Children's Cancer Group study of 252 patients with acute myeloid leukemia. *Blood*. 2003;101(9):3398-3406.

42. Belov L, Mulligan SP, Barber N, et al. Analysis of human leukaemias and lymphomas using extensive immunophenotypes from an antibody microarray. *Br J Haematol*. 2006;135(2):184-197.

43. Chopra A, Pati H, Mahapatra M, et al. Flow cytometry in myelodysplastic syndrome: analysis of diagnostic utility using maturation pattern-based and quantitative approaches. *Ann Hematol*. 2012;91(9):1351-1362.

44. Kanbe K, Inoue K, Inoue Y, Suzuki Y. Histological changes in bone marrow after treatment of infliximab for rheumatoid arthritis. *Clin Rheumatol*. 2008;27(4):497-501.

45. Krnjacki LJ, Baade PD, Lynch BM, Aitken JF. Reliability of collecting colorectal cancer stage information from pathology reports and general practitioners in Queensland. *Aust N Z J Public Health*. 2008;32(4):378-382.

46. Lewis DK, Whitty CJM, Epino H, Letsky EA, Mukiibi JM, van den Broek NR. Interpreting tests for iron deficiency among adults in a high HIV prevalence African setting: routine tests may lead to misdiagnosis. *Trans R Soc Trop Med Hyg*. 2007;101(6):613-617.

47. Maurillo L, Buccisano F, Spagnoli A, et al. Monitoring of minimal residual disease in adult acute myeloid leukemia using peripheral blood as an alternative source to bone marrow. *Haematologica*. 2007;92(5):605-611.

48. Oh HS, Choi J-H, Park CK, et al. Comparison of microvessel density before and after peripheral blood stem cell transplantation in multiple myeloma patients and its clinical implications: multicenter trial. *Int J Hematol*. 2002;76(5):465-470.

49. Raynaud P, Caulet-Maugendre S, Foussard C, et al. T-cell lymphoid aggregates in bone marrow after rituximab therapy for B-cell follicular lymphoma: a marker of therapeutic efficacy? *Hum Pathol*. 2008;39(2):194-200.

50. Rowe JM, Kim HT, Cassileth PA, et al. Adult patients with acute myeloid leukemia who achieve complete remission after 1 or 2 cycles of induction have a similar prognosis: a report on 1980 patients registered to 6 studies conducted by the Eastern Cooperative Oncology Group. *Cancer*. 2010;116(21):5012-5021.

51. Takasaki Y, Iwanaga M, Tsukasaki K, et al. Impact of visceral involvements and blood cell count abnormalities on survival in adult T-cell leukemia/lymphoma (ATLL). *Leuk Res*. 2007;31(6):751-757.

52. Tsan CJ, Serpell JW, Poh YY. The impact of synoptic cytology reporting on fine-needle aspiration cytology of thyroid nodules. *ANZ J Surg*. 2007;77(11):991-995.

53. Vance GH, Kim H, Hicks GA, et al. Utility of interphase FISH to stratify patients into cytogenetic risk categories at diagnosis of AML in an Eastern Cooperative Oncology Group (ECOG) clinical trial (E1900). *Leuk Res*. 2007;31(5):605-609.

54. Wang W, Wang X, Xu X, Lin G. Diagnosis and treatment of acquired aplastic anaemia in adults: 142 cases from a multicentre, prospective cohort study in Shanghai, China. *J Int Med Res*. 2011;39(5):1994-2005.

55. Wiedswang G, Borgen E, Karesen R, et al. Detection of isolated tumor cells in bone marrow is an independent prognostic factor in breast cancer. *J Clin Oncol*. 2003;21(18):3469-3478.

56. Wilkins BS, Erber WN, Bareford D, et al. Bone marrow pathology in essential thrombocythemia: interobserver reliability and utility for identifying disease subtypes. *Blood*. 2008;111(1):60-70.

57. Aumann K, Amann D, Gumpp V, et al. Template-based synoptic reports improve the quality of pathology reports of prostatectomy specimens. *Histopathology*. 2012;60(4):634-644.

58. Austin R, Thompson B, Coory M, Walpole E, Francis G, Fritschi L. Histopathology reporting of breast cancer in Queensland: the impact on the quality of reporting as a result of the introduction of recommendations. *Pathology (Phila)*. 2009;41(4):361-365.

59. Barbui T, Thiele J, Passamonti F, et al. Initial bone marrow reticulin fibrosis in polycythemia vera exerts an impact on clinical outcome. *Blood*. 2012;119(10):2239-2241.

60. Baumann I, Fuhrer M, Behrendt S, et al. Morphological differentiation of severe aplastic anaemia from hypocellular refractory cytopenia of childhood: reproducibility of histopathological diagnostic criteria. *Histopathology*. 2012;61(1):10-17.

61. Beattie GC, McAdam TK, Elliott S, Sloan JM, Irwin ST. Improvement in quality of colorectal cancer pathology reporting with a standardized proforma--a comparative study. *Colorectal Dis*. 2003;5(6):558-562.

62. Chan NG, Duggal A, Weir MM, Driman DK. Pathological reporting of colorectal cancer specimens: a retrospective survey in an academic Canadian pathology department. *Can J Surg*. 2008;51(4):284-288.

63. Gallamini A, Stelitano C, Calvi R, et al. Peripheral T-cell lymphoma unspecified (PTCL-U): a new prognostic model from a retrospective multicentric clinical study. *Blood*. 2004;103(7):2474-2479.

64. Gandemer V, Auclerc M-F, Perel Y, et al. Impact of age, leukocyte count and day 21-bone marrow response to chemotherapy on the long-term outcome of children with philadelphia chromosome-positive acute lymphoblastic leukemia in the pre-imatinib era: results of the FRALLE 93 study. *BMC Cancer*. 2009;9:14.

65. Gianelli U, Vener C, Bossi A, et al. The European Consensus on grading of bone marrow fibrosis allows a better prognostication of patients with primary myelofibrosis. *Mod Pathol*. 2012;25(9):1193-1202.

66. Howell SJ, Grey M, Chang J, et al. The value of bone marrow examination in the staging of Hodgkin's lymphoma: a review of 955 cases seen in a regional cancer centre. *Br J Haematol*. 2002;119(2):408-411.

67. Kvasnicka HM, Thiele J. The impact of clinicopathological studies on staging and survival in essential thrombocythemia, chronic idiopathic myelofibrosis, and polycythemia rubra vera. *Semin Thromb Hemost*. 2006;32(4 Pt 2):362-371.

68. Lugli A, Ebnoether M, Cogliatti SB, et al. Proposal of a morphologic bone marrow response score for imatinib mesylate treatment in chronic myelogenous leukemia. *Hum Pathol*. 2005;36(1):91-100.

69. Mhawech-Fauceglia P, Oberholzer M, Aschenafi S, et al. Potential predictive patterns of minimal residual disease detected by immunohistochemistry on bone marrow biopsy specimens during a long-term follow-up in patients treated with cladribine for hairy cell leukemia. *Arch Pathol Lab Med*. 2006;130(3):374-377.

70. Shearer BM, Sukov WR, Flynn HC, Knudson RA, Ketterling RP. Development of a dual-color, double fusion FISH assay to detect RPN1/EVI1 gene fusion associated with inv(3), t(3;3), and ins(3;3) in patients with myelodysplasia and acute myeloid leukemia. *Am J Hematol*. 2010;85(8):569-574.

71. Gill AJ, Johns AL, Eckstein R, et al. Synoptic reporting improves histopathological assessment of pancreatic resection specimens. *Pathology (Phila).* 2009;41(2):161-167.

72. Harvey JM, Sterrett GF, McEvoy S, et al. Pathology reporting of breast cancer: trends in 1989-1999, following the introduction of mammographic screening in Western Australia. *Pathology (Phila)*. 2005;37(5):341-346.

73. Hassell L, Aldinger W, Moody C, et al. Electronic capture and communication of synoptic cancer data elements from pathology reports: results of the Reporting Pathology Protocols 2 (RPP2) project. *J Reg Manag*. 2009;36(4):117-124; quiz 163-115.

74. Haugland HK, Casati B, Dorum LM, Bjugn R. Template reporting matters--a nationwide study on histopathology reporting on colorectal carcinoma resections. *Hum Pathol*. 2011;42(1):36-40.

75. Idowu MO, Bekeris LG, Raab S, Ruby SG, Nakhleh RE. Adequacy of surgical pathology reporting of cancer: a College of American Pathologists Q-Probes study of 86 institutions. *Arch Pathol Lab Med*. 2010;134(7):969-974.

76. Karim RZ, van den Berg KS, Colman MH, McCarthy SW, Thompson JF, Scolyer RA. The advantage of using a synoptic pathology report format for cutaneous melanoma. *Histopathology*. 2008;52(2):130-138.

77. King PM, Blazeby JM, Gupta J, Alderson D, Moorghen M. Upper gastrointestinal cancer pathology reporting: a regional audit to compare standards with minimum datasets. *J Clin Pathol*. 2004;57(7):702-705.

78. Kussick SJ, Wood BL. Using 4-color flow cytometry to identify abnormal myeloid populations. *Arch Pathol Lab Med*. 2003;127(9):1140-1147.

79. Kwon JS, Francis JA, Qiu F, Weir MM, Ettler HC. When is a pathology review indicated in endometrial cancer? *Obstet Gynecol*. 2007;110(6):1224-1230.

80. Lane S, Saal R, Mollee P, et al. A >or=1 log rise in RQ-PCR transcript levels defines molecular relapse in core binding factor acute myeloid leukemia and predicts subsequent morphologic relapse. *Leuk Lymphoma*. 2008;49(3):517-523.

81. Maly E, Przyborsk M, Nowak T, Nowak J, Januszkiewicz D. FLT3 internal tandem duplication and FLT3-D835 mutation in 80 AML patients categorized into cytogenetic risk groups. *Postepy Hig Med Dosw (Online).* 2010;64:466-470.

82. Martinez A, Ponzoni M, Agostinelli C, et al. Primary bone marrow lymphoma: an uncommon extranodal presentation of aggressive non-hodgkin lymphomas. *Am J Surg Pathol*. 2012;36(2):296-304.

83. Moid F, DePalma L. Comparison of relative value of bone marrow aspirates and bone marrow trephine biopsies in the diagnosis of solid tumor metastasis and Hodgkin lymphoma: institutional experience and literature review. *Arch Pathol Lab Med*. 2005;129(4):497-501.

84. Schanz J, Steidl C, Fonatsch C, et al. Coalesced multicentric analysis of 2,351 patients with myelodysplastic syndromes indicates an underestimation of poor-risk cytogenetics of myelodysplastic syndromes in the international prognostic scoring system. *J Clin Oncol*. 2011;29(15):1963-1970.

85. Thiele J, Kvasnicka HM, Schmitt-Graeff A, Diehl V. Dynamics of fibrosis in chronic idiopathic (primary) myelofibrosis during therapy: a follow-up study on 309 patients. *Leuk Lymphoma*. 2003;44(6):949-953.

86. Giri N, Alter BP, Peredo-Pinto H, et al. Significance of bone marrow karyotype and morphology in patients with inherited bone marrow failure syndromes [ASH meeting abstract]. *Blood*. 2011;118(21):3431.

87. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. *Blood*. 2012;120(12):2454-2465.

88. Kao JM, McMillan A, Greenberg PL. International MDS risk analysis workshop (IMRAW)/IPSS reanalyzed: impact of cytopenias on clinical outcomes in myelodysplastic syndromes. *Am J Hematol*. 2008;83(10):765-770.

89. Kent SA, Variakojis D, Peterson LC. Comparative study of marginal zone lymphoma involving bone marrow. *Am J Clin Pathol*. 2002;117(5):698-708.

90. Liu D, Chen Z, Xue Y, et al. The significance of bone marrow cell morphology and its correlation with cytogenetic features in the diagnosis of MDS-RA patients. *Leuk Res*. 2009;33(8):1029-1038.

91. Messenger DE, McLeod RS, Kirsch R. What impact has the introduction of a synoptic report for rectal cancer had on reporting outcomes for specialist gastrointestinal and nongastrointestinal pathologists? *Arch Pathol Lab Med*. 2011;135(11):1471-1475.

92. Musolino A, Guazzi A, Nizzoli R, Panebianco M, Mancini C, Ardizzoni A. Accuracy and relative value of bone marrow aspiration in the detection of lymphoid infiltration in non-Hodgkin lymphoma. *Tumori*. 2010;96(1):24-27.

93. Persing S, James TA, Mace J, Goodwin A, Geller B. Variability in the quality of pathology reporting of margin status following breast cancer surgery. *Ann Surg Oncol*. 2011;18(11):3061-3065.

94. Siragusa S, Morice W, Gertz MA, et al. Asymptomatic immunoglobulin light chain amyloidosis (AL) at the time of diagnostic bone marrow biopsy in newly diagnosed patients with multiple myeloma and smoldering myeloma. A series of 144 cases and a review of the literature. *Ann Hematol*. 2011;90(1):101-106.

95. Thiele J, Kvasnicka HM, Mullauer L, Buxhofer-Ausch V, Gisslinger B, Gisslinger H. Essential thrombocythemia versus early primary myelofibrosis: a multicenter study to validate the WHO classification. *Blood*. 2011;117(21):5710-5718.

96. Turkington RC, Arnold EC, Percy MJ, Ranaghan LA, Cuthbert RJ, McMullin MF. Comparison of diagnostic criteria for polycythaemia vera. *Hematology*. 2007;12(2):123-130.

97. Turner JJ, Hughes AM, Kricker A, et al. WHO non-Hodgkin's lymphoma classification by criterion-based report review followed by targeted pathology review: an effective strategy for epidemiology studies. *Cancer Epidemiol Biomarkers Prev*. 2005;14(9):2213-2219.

98. Verleye L, Ottevanger PB, Kristensen GB, et al. Quality of pathology reports for advanced ovarian cancer: are we missing essential information? An audit of 479 pathology reports from the EORTC-GCG 55971/NCIC-CTG OV13 neoadjuvant trial. *Eur J Cancer*. 2011;47(1):57-64.

99. Yunker WK, Matthews TW, Dort JC. Making the most of your pathology: standardized histopathology reporting in head and neck cancer. *J Otolaryngol Head Neck Surg*. 2008;37(1):48-55.

100. Janni W, Rack B, Kasprowicz N, Scholz C, Hepp P. DTCs in breast cancer: clinical research and practice. *Recent Results Cancer Res*. 2012;195:173-178.

101. Garcia-Manero G. Myelodysplastic syndromes: 2012 update on diagnosis, risk-stratification, and management. *Am J Hematol*. 2012;87(7):692-701.

102. College of American Pathologists. Synoptic Report Definition and Examples. College of American Pathologists website. http://www.cap.org/ShowProperty?nodePath=/UCMCon/Contribution%20Folders/WebContent/pdf/synoptic-definition-and-examples.pdf. Updated August 26, 2015. Accessed October 28, 2015.

103. Teutsch SM, Bradley LA, Palomaki GE, et al. The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) Initiative: methods of the EGAPP Working Group. *Genet Med*. 2009;11(1):3-14.

104. Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *PLoS Med*. 2009;6(7):e1000097.