Use of CME to impact self-reported changes in the evaluation and management of anaemia in geriatric patients

Kathleen Farmer1, Betsy Dennison2, Paul D. Walden2, Brian Koffman3, David P. Steensma4 and Jill Hays1

Abstract

Objective. The Third US National Health and Nutrition Examination Survey (NHANES III) prompted the recognition of geriatric anaemia as a public health concern since ~10% of people aged 65 years or older were anaemic. The objective of this study was to design and implement a continuing medical education (CME) event that motivates and guides Primary Care Health Practitioners (PCHPs) to adopt medical practices that improve outcomes among geriatric patients with anaemia by employing effective diagnostic workup. Research design and methods. A total of 4196 PCHPs participated in 11 highly interactive 75-minute live conferences conducted throughout the US from 2011 through 2013 that featured case-based interactive discussions on the workup of microcytic, normocytic, and macrocytic anaemia by a PCHP and local haematologist expert. A standardised diagnostic algorithm for geriatric anaemia was used and distributed as a handout at the live activity. A reinforcing mobile application based on this algorithm was introduced in 2012. Main outcome measures. Data from participants were gathered immediately after the event, 10–12 weeks post-event, and 1–3 years post-event. Outcomes were evaluated according to Moore’s levels. Chi-squared analyses compared the proportion of respondents who committed to one or more of the five major behavioural changes over time. Results. The Chi-squared test analysed data from each of the three timelines for five medical behavioural changes. A comparison of participants’ responses showed that there was a significant increase in the proportion of responders committing to behavioural change #1, “Avoid indiscriminant use of erythropoiesis-stimulating agents” and #5, “Refer patients with unexplained mild anaemia to a haematologist” from post-event to 1–3 years (p<0.001) (see Table 2). The proportion of respondents who committed to the other three behavioural changes remained consistent over time, suggesting that actual change in medical practice occurred at 1–3 years. Conclusions. This proof of concept study validates the use of case-based CME involving a highly interactive discussion between PCHP and specialist, used in conjunction with a standardised diagnostic algorithm as effective in improving PCHP knowledge, competence, and self-reported performance improvement. This study lays the groundwork for follow-up studies using objective performance measures.

Keywords: CME, impact, change in practice behaviours

Introduction

In the Third US National Health and Nutrition Examination Survey (NHANES III, 1988–1994), approximately 10% (~3 million) of people aged 65 years or older were anaemic1 as defined by the World Health Organisation as a haemoglobin...
of <12 g/dL for women and <13 g/dL for men.\(^3\) Within this population, one-third had unexplained anaemia. Based on the significance of this finding, the American Society of Haematology (ASH), in conjunction with the National Institute of Aging (NIA), convened a panel of 20 experts in haematology and geriatrics in March 2004, to address the question of anaemia in the elderly in the United States.\(^3\)

A conclusion was that Primary Care Health Providers (PCHPs), as the primary gatekeepers for entry into the healthcare system, needed continuing medical education (CME) to learn and follow an anaemia algorithm for early screening, diagnosing, management, and referral when indicated. With the introduction of the Patient Protection and Affordable Care Act (PPACA),\(^4\) this need became even more important.

Via a survey, a random sample of 190 Massachusetts PCHPs were presented with a vignette concerning a patient with a new finding of moderate anaemia, and then asked what they would do if the patient returned with persistent anaemia plus one additional sign or symptom.\(^5\) Among the 134 (70.5%) PCHPs who responded, only 3.8% reported referring to a haematologist at the first anaemia presentation. The development of a second sign or symptom suggestive of myelodysplastic syndrome (MDS) or leukaemia most often prompted early referral, while those suggesting lymphoma were generally followed by imaging. While clinically reasonable, this approach may delay diagnosis and treatment by haematological specialists. The study also found that several lower-cost and effective laboratory tests (e.g., reticulocyte count) were relatively underutilised, while over 25% reported obtaining colonoscopy as a first step. Taken together, the findings from this study suggest that utilisation of a diagnostic anaemia protocol by PCHPs would improve healthcare delivery in a manner that is aligned with the so-called “Triple Aim” concept of 1) improving the experience of care, 2) improving the health of populations, and 3) reducing per capita costs of health care.\(^6\)

Medical education providers have been challenged by the Institute of Medicine (IOM) to design CME/CE activities that address the professional needs of PCHPs and facilitate their adoption of protocols or algorithms into their medical practice.\(^7\) Primary Care Network (PCN) partnered with Clarity Communication to design a CME/CE activity that targets primary care clinicians: medical doctors (MDs), doctors of osteopathy (DOs), nurse practitioners (NPs), and physician assistants (PAs) with the goal of improving their medical practice concerning screening and managing geriatric anaemia through presenting an algorithm, developed by leading experts, Steensma and Tefferi.\(^8\) The activity was created around professional gaps, needs assessment, and objectives as indicated from a survey of PCN’s members, haematology experts, and scientific data (see Table 1). Following adult learning principles and Cognitive Load Theory,\(^9\) a variety of educational venues were employed to communicate and achieve the event’s objectives. These included case studies, audience response system (ARS) questions, and spirited presentations onstage by a primary care physician and a haematologist. The objectives in this article are to describe the development and implementation process and assess the effect on self-reported clinical practice changes.

### Table 1. Learning objectives for the live conferences and their relationship to identified gaps in care.

| Professional practice gap 1 | What is happening | Anaemia is often considered a normal part of the aging process. |
|----------------------------|-------------------|---------------------------------------------------------------|
| What should happen         | Anaemia should neither be considered normal nor harmless and may have far-reaching effects. |
| Professional practice gap 2 | What is happening | Geriatric anaemia is not being fully evaluated which may lead to adverse outcomes due to delayed diagnosis of potentially treatable conditions and increased risk of death and certain comorbidities. |
| What should happen         | Once a diagnosis of anaemia has been made from the patient’s symptoms or incidental blood test, geriatric anaemia should be evaluated using many of the same principles used for younger patients. |
| Professional practice gap 3 | What is happening | Appropriate treatment plans are often not fully investigated which may result in under treatment of easily treatable conditions, over-referral to GI specialists, and conversely under recognition of conditions requiring referral to a haematologist. |
| What should happen         | Geriatric patients with anaemia are managed in a timely and effective manner including appropriate referral to a specialist. |

### Learning objectives

- **Professional practice gap 1**: Differentiate among the etiological causes of anaemia seen in geriatric patients.
- **Professional practice gap 2**: Develop appropriate workup of elderly patients diagnosed with symptomatic anaemia or anaemia detected by incidental blood testing.
- **Professional practice gap 3**: Incorporate strategies to manage elderly patients with anaemia due to iron deficiency, nutritional deficiency or chronic disease, and determine when it is appropriate to refer to a haematologist or gastroenterologist for further evaluation.
Rationale
The authors of this manuscript had previously shown, in a retrospective analysis of claims data from a large US payer, that CME could be used as an intervention tool to reduce time from a non-specific diagnosis of anaemia to a specific diagnosis of anaemia due to MDS. In this prospective study, the goal was to use CME to change knowledge, competency, and performance to improve the diagnostic efficacy and workup of geriatric anaemia by PCHPs in alignment with the triple aims described above. The desired changes resulting from this CME intervention were for PCHPs to:

- Recognise the common causes of anaemia in geriatric patients and the consequences of failure to treat (knowledge)
- Implement the initial and subsequent steps involved in the workup of geriatric patients with anaemia to determine appropriate management following a diagnostic algorithm (knowledge, competency)
- Manage geriatric patients with various causes of anaemia (knowledge, competency)
- Employ the appropriate workup for anaemia in geriatric patients based upon the knowledge of causes (knowledge, competence, performance)
- Refer to a specialist when indicated (knowledge, competence, performance)

Research design and methods

CME intervention
A series of 11 highly interactive 75-minute live conferences was conducted throughout the US during 2011 through 2013. The study population, participants in the live conferences, was identified through registration and evaluation forms post-event and comprised MDs/DOs (68%), NPs/PAs (30%), and Other (2%).

PCN accredited each activity for AMA PRA Category 1 Credit™, as well as American Academy of Family Physicians (AAFP) and American Association of Nurse Practitioners (AANP) credit. The live conferences were designed around adult learning principles and featured three case-based interactive discussions on the workup of microcytic, normocytic, and macrocytic anaemia by a PCHP and local haematology expert. A diagnostic algorithm for geriatric anaemia was used and distributed as a handout at the haematology expert. A diagnostic algorithm for geriatric normocytic, and macrocytic anaemia by a PCHP and local based interactive discussions on the workup of microcytic, around adult learning principles and featured three case-tioners (AANP) credit. The live conferences were designed for referrals and for additional questions.

In October 2012, a mobile application based on the diagnostic algorithm for geriatric anaemia was developed as an additional resource to reinforce behaviour change as a result of the live CME event (Fig. 2). PCN created awareness of the application by emailing monthly announcements to their entire database of 65,000 members, as well as promoting it during the live anaemia CME activities.

Learning objectives
The learning objectives for this activity were based on consensus gaps in care identified by the ASH, the NIA, and haematology experts, and an initial survey was sent to PCN members. Table 1 shows a listing of the learning objectives for the live conference and their connection to the underlying gaps in care.

Outcomes measurement
Outcomes were measured according to Moore’s seven levels: Participation; Satisfaction; Learning; Competence; Performance; Patient Health; and Community Health. There were a total of 4196 participants in the 11 live conferences. An ARS was used throughout the conferences to assess audience demographics, baseline knowledge, and knowledge change resulting from the activity (pre- and post-test). Changes in competence were evaluated by a commitment to change question that was included on the programme evaluation form and administered immediately after the live activity. This question probed for planned changes to practice based on learning from the conference. Self-reported changes in performance were evaluated by administering a post-programme survey which asked whether the education was integrated into clinical practice and whether attendees performed anaemia-specific medical practice behaviours more, the same, or less than they did prior to the educational activity. These surveys were emailed to participants at 10–12 weeks after the live event and the response rate was 10%. Another follow-up survey was emailed 1–3 years after the live event (response rate 2%).

Statistical methods
Data were collected immediately after the CME event on a pencil-and-paper evaluation form (for participants to receive CME credit) and on electronic surveys at 10–12 weeks and 1–3 years post-event. The electronic survey at 1–3 years informed the responders that the data would be used for a platform presentation at the Alliance meeting in January 2015. By responding, the responders gave the researchers permission to analyse and present the data they provided. The Chi-squared test analysed aggregate data; individual responders were de-identified. Data were analysed from each of the three timelines for five medical behavioural changes. The data were unpaired; a recent study found no significant differences between paired and unpaired data, meaning that unpaired data are valuable predictors of total competency improvements (see Table 2).

Results
There were a total of 4196 participants across 11 live conferences from 2011 to 2013. Outcomes were evaluated according to Moore’s Levels.
Level 1 Participation
Demographics were tracked through registration and evaluation forms: MD/DO 68%; NP/PA 30%; Other 2%.

Level 2 Satisfaction
Ninety-six percent of attendees rated the speakers as excellent or very good, indicated that the learning objectives were met, and that the activities were free of commercial bias.

Level 3 Learning
Through case-based learning, an overall 76% relative increase in knowledge, skills, and/or confidence resulted from the education.

- 76% relative increase in knowledge of the test that is diagnostically most useful in narrowing the differential diagnosis of geriatric anaemia (mean corpuscular volume or MCV) (55% pre-test vs. 96% post-test)
- 186% relative increase in knowledge of the test that is most sensitive to the presence of a combined nutritional deficiency (red cell distribution width or RDW) (26% pre-test vs. 74% post-test)
- 148% relative increase in knowledge that older patients with anaemia are at higher risk for all the following (major depression, decreased bone density, decreased skeletal muscle mass, and poorer cognition) except poorly controlled type 2 diabetes (37% pre-test vs. 92% post-test)
- 115% relative increase in knowledge that referral to a haematologist is the appropriate next step in the workup of a 66-year-old female presenting with anaemia and macrocytosis, with otherwise negative history, physical, and laboratory work (43% pre-test vs. 93% post-test)
- 157% relative increase in knowledge that for a patient with microcytic anaemia, the most likely differential diagnoses would include all of the following (iron deficiency, anaemia of chronic inflammation, or haemoglobin E trait) except a bone marrow disorder, especially MDS (28% pre-test vs. 71% post-test)

Level 4 Competence
Changes in competence were evaluated by a commitment to change question that was included on the programme evaluation form and administered immediately after the
Upon returning to my practice, I plan to... (Table 2). Of note 47% of participants committed to use the provided algorithm, 44% committed to determining MCV and performing iron studies before referral, and 55% committed to perform follow-up laboratory investigation before referral to GI or haematology.

Level 5 Performance

Self-reported performance changes were evaluated by following up on the commitment to change question 10–12 weeks post-activity and 1–3 years post-activity (Table 2). At 1–3 years post-activity, 54% of survey respondents reported using the algorithm, 64% reported they determine MCV and perform iron studies prior to referral and 66% reported they perform follow-up laboratory tests before referral to gastroenterology or haematology (see Table 2 and Fig. 3).

Chi-squared analyses of the respondents’ commitment to change over time indicated that there were significant increases in the proportion of respondents who committed to five behavioural changes at 10–12 weeks post-activity compared to the responses immediately after the event (p<0.001). When comparing the proportion of respondents who committed to change at 1–3 years compared to the responses immediately after the event, there were two behavioural changes that reached significance (“Avoid indiscriminant use of erythropoiesis-stimulating agents” and “Refer patients with unexplained... ”).
When comparing the proportion of respondents who committed to change at 1–3 years compared to the responses at 10–12 weeks, a significant decrease was found only for “The use of the algorithm”; \( p=0.003 \); see Table 2.

As of August 31, 2014, there had been 14,000 downloads from Apple’s iTunes Store (iPhone or iPad) or the Google Play Store (Android) worldwide, which suggests that many clinicians found the mobile application useful to their practice and that the application may have contributed to behaviour change.

*Numbers varied by practice behaviour as respondents were able to respond “Not Yet” or “Not applicable to my practice.”

Commitment to change: comparisons over-time Chi-squared

| Behavioural change | Post-activity/10–12 weeks | Post-activity/1–3 years | 10–12 weeks/1–3 years |
|--------------------|---------------------------|-------------------------|------------------------|
| Avoid indiscriminant use of ESAs | Increase in proportion of responders committing to behavioural change \( p=0.001 \) | Increase in proportion of responders committing to behavioural change \( p=0.001 \) | Increase in proportion of responders committing to behavioural change \( p=0.003 \) |
| Use the algorithm | Significant change \( p=0.001 \) | No significant change \( p=0.26 \) | Significant decrease \( p=0.17 \) |
| Determine MCV and perform iron studies before referral | Significant change \( p=0.001 \) | No significant change \( p=0.13 \) | No significant change \( p=0.11 \) |
| Perform follow-up laboratory tests before referral to GI or haematology | Significant change \( p=0.001 \) | Significant change \( p=0.001 \) | No significant change \( p=0.12 \) |
| Refer patients with unexplained mild anaemia to a haematologist | Significant change \( p=0.001 \) | Significant change \( p=0.001 \) | No significant change \( p=0.12 \) |

As of August 31, 2014, there had been 14,000 downloads from Apple’s iTunes Store (iPhone or iPad) or the Google Play Store (Android) worldwide, which suggests that many clinicians found the mobile application useful to their practice and that the application may have contributed to behaviour change.

Figure 3. Self-reported medical practice changes over time. Percentage of commitments addressing the five medical practice changes in categories that were not implemented, those that were at least partially implemented, and those who found the changes not applicable to their practice by study participants.
Level 6 Patient health
On the 1–3 years post-activity survey, two additional questions were asked that served as a self-reported surrogate for changes in patient health: 48% of respondents believe that implementation of the anaemia-specific medical practice behaviours improved outcomes among geriatric patients and 60% who adopted anaemia-specific medical practice behaviours believe that assessment and management of anaemia reduced time required for evaluation and determination of studies to order.

Discussion
The authors describe the process of designing and implementing an interactive, multimedia, multidisciplinary, collaborative CME/CE activity on geriatric anaemia for primary care clinicians in 11 cities across the United States. Adult learning principles and the Cognitive Load Theory,9 that is, building on participants’ present knowledge to expand their medical practice behaviours, were the foundation of the activity.

Within the framework of Adult Learning Principles, Knowles formulated five steps to enhance learning among adults13: 1) Why the topic is important; 2) Material is presented visually, auditorily, and kinesthetically; 3) Incorporate knowledge into learners’ experiences; 4) The learner is receptive; 5) The event is positive. The ARS was a measure of the level of knowledge the participant demonstrated in geriatric anaemia and where the individual’s responses ranked in the audience’s knowledge. Also, post-event the ARS informed the participant how much more knowledge was learned during the 75-minute CME event. The animated power point presentation and interchange between primary care physician and haematologist onstage incorporated knowledge through multiple sensory mechanisms. Case studies within the didactic part of the event put a face on the problem of geriatric anaemia, inserting knowledge into the participants’ clinical experience, past and future. The standardised diagnostic algorithm was a take-away reminder and clinical support for screening, diagnosing, and managing geriatric anaemia. The get-together after the event was an opportunity for the participant to interact with a local haematologist about problem patients and questions concerning referral and follow-up.

The data suggest that this event is associated with clinical practice changes and significant improvements in identifying, managing, and referring geriatric anaemic patients.

This is the first study to measure the impact of CME/CE on medical practice changes 1–3 years after a 75-minute event. Most studies limit the impact of CME/CE to 3 months post-activity. Also, the audience was large and multidisciplinary. Most other studies include physicians with only a small number of participants. In addition, the medical practice behaviour changes were directly linked to the objectives of the educational event, unlike most studies that identify “unanticipated learning” that are behavioural changes not part of the educational objectives.14

The findings of the statistical analyses were surprising to the authors. It was expected that there would be no significant differences in adopting medical practice behaviours for geriatric anaemia over time; that the proportion of those who committed to change would be the same over time. The finding that there were two behavioural changes subscribed by a greater proportion of respondents from immediate post-activity to 1–3 years post-activity suggests that indeed the commitment to change evolved into an actual change in practice behaviour. In analysing the data from 10–12 weeks to 1–3 years, the significant decrease in the use of the algorithm may have been the reflection of confusion over the printed anaemia algorithm handed out at the event and the electronic anaemia app that was downloadable from Apple’s iTunes Store that was presented in 2012. This may be verified by the data, comparing the use of the algorithm from immediately after the event to 1–3 years post-event, which showed no significant change in the use of the algorithm.

This study has three main limitations. The outcomes were self-reported without a control group and without independent verification of actual changes in medical practice. The study population who responded to surveys dropped from 100% (immediately after the CME event) to 10% (at 10–12 weeks post-event) and finally to 2% (at 1–3 years post-event). The assumption was that the individuals who responded to the electronic survey 1–3 years after the event indeed changed their medical practice behaviours concerning diagnosing and managing geriatric anaemia. This has been verified in two studies and one review that demonstrated that physicians who expressed a commitment to change were significantly more likely to change.15–17 However, due to the low response rate at 1–3 years post-event, there may be a bias due to self-selection.

Conclusion
Given that PCHPs serve as the primary gatekeepers for entry into the healthcare system, they represent an important population for CME. The NHANES III study showed geriatric anaemia to be a public health concern11,12 and a recent survey of PCHPs suggested that utilisation of diagnostic anaemia protocols by PCHPs could improve healthcare delivery in a manner that is aligned to the improvement of the health of geriatric anaemia populations, and reducing costs of health care.6 Our study has shown that CME is an effective conduit to increase PCHPs’ knowledge and competency of the aetiology, workup and management of geriatric anaemia. Based on our experience, incorporating a standardised diagnostic algorithm and presenting practical information as part of a highly interactive discussion between a PCHP and haematology specialist were critical success factors in the CME implementation. We built upon this success by developing a mobile application based on this diagnostic algorithm that provides a useful resource that can be used at point-of-service (POS) or otherwise in the workup of geriatric patients with anaemia.
Among the 2% of CME participants who responded to the electronic survey 1–3 years post-event, there appears to be a maintenance of change that may be an indication of a behavioural transformation that is occurring, or has occurred, due to a combination of participating in the live activity, followed by reinforcement with continued learning, use of the mobile application or patient interaction in daily clinical practice. Maintenance is considered the epitome of the five stages of behavioural change: Pre-contemplation, Contemplation, Preparation, Action Learning and Maintenance.18

This study was designed as a proof of concept to act as a segue to further studies that can address improvement in healthcare. Future studies could include objective measures of performance change such as analysis of electronic health records, payer claims or haematology referrals for participating PCHPs who consent to the use of this information. A future study should also include a control group comprising PCHPs with similar demographics who did not attend the CME activity.

Disclosures

DPS serves on the Advisory Board for Celgene and is a consultant for Amgen, Eisai, Inc.

BK serves on the Advisory Board for AstraZeneca and ResMed. He is a consultant for Janssen Pharmaceuticals, Inc. and a Patient Speaker for Pharmacyclics. He serves on the Speaker’s Bureau for AstraZeneca and is a share stockholder for AbbVie, Incyte, Gilead, Pharmacyclics and TGTX.

KF, BD, PDW, JH have no relevant financial relationships.

Acknowledgements

The educational activities and mobile application mentioned in this article were supported by an independent medical educational grant from Celgene. The authors acknowledge the editorial and statistical contributions of Candace Shade and Heather Manley.

References

1. Guralnik JM, Eisenstaedt RS, Ferrucci L, Klein HG, Woodson RC. Prevalence of anaemia in persons 65 years and older in the United States: evidence for a high rate of unexplained anaemia. Blood 2004;104: 2263–2268.

2. Nutritional anemias. Report of a WHO scientific group. World Health Organ Tech Rep Ser 1968;405:5–37.

3. Guralnik JM, Ershler WB, Schrier SL, Picozzi VJ. Anaemia in the elderly: a public health crisis in haematology. Haematology Am Soc Hematol Educ Program 2005;1:528–532.

4. Patient Protection and Affordable Care Act of 2010, Pub. L. No. 111-148, 124 Stat. 119, amended by Health Care and Education Reconciliation Act of 2010, Pub. L. No. 111–152, 124 Stat. 1029.

5. Abel GA, Friese CR, Neville BA, Wilson KM, Hastings BT, Earle CC, et al. Referrals for suspected hematologic malignancy: a survey of primary care physicians. Am J Hematol 2012;87:634–636.

6. Agency for Healthcare Research and Quality. Working for quality: About the National Quality Strategy (NQS). Available at: http://www.ahrq.gov/workingforquality/about.htm, accessed January 24, 2015.

7. Adams SG, Pitts J, Wynne J, Yawn BP, Diamond EJ, Lee S, et al. Effect of a primary care continuing education program on clinical practice of chronic obstructive pulmonary disease: translating theory in practice. Mayo Clin Proc 2012;87:862–870.

8. Steensma DP, Telfer E. Anaemia in the elderly: how should we define it, when does it matter, and what can be done? Mayo Clin Proc 2007;82:958–966.

9. Young JQ, Van Merrienboer J, Durning S, Cate OT. Cognitive Load Theory: implications for medical education: AMEE Guide No. 86. Med Teach 2014;36:371–384.

10. Walden PD, Dennison B, Hane C, Yezelzman A, Baldwin A, Moore V, et al. Administrative health data to assess performance in a myelodysplastic syndromes CME initiative. CE Meas 2010;4:26–33.

11. Moore DE, Jr., Green JS, Gallis HA. Achieving desired results and improved outcomes: integrating planning and assessment throughout learning activities. J Contin Educ Health Prof 2009;29:1–15.

12. Heintz A, Fagerlie SR. Competence assessments: to pair or not to pair: that is the question. Platform presentation. Alliance for Continuing Education in the Health Professions (ACEHP) Convention, Grapevine, Texas, January; 2015.

13. Knowles M, Holton EF, Swanson RA. The adult learner: the definitive classic in adult education and human resource development (6th ed.). Burlington, MA: Elsevier; 2005.

14. Dolcourt JL, Zuckerman G. Unanticipated learning outcomes associated with commitment to change in continuing medical education. J Contin Educ Health Prof 2003;23:173–181.

15. Wakefield J, Herbert CP, Maclure M, Dormuth C, Wright JM, Legare J, et al. Commitment to change statements can predict actual change in practice. J Contin Educ Health Prof 2003;23:81–93.

16. Curry L, Purkis IE. Validity of self-reports of behavior changes by participants after a CME course. J Med Educ 1986;61:579–584.

17. Wakefield JG. Commitment to change: exploring its role in changing physician behavior through continuing education. J Con Educ in Health Prof 2014;24:197–204.

18. Prochaska JO, DiClemente CC. Stages and processes of self-change of smoking: toward an integrative model of change. J Consult Clin Psychol 1983;51:390–5.

19. Zakai NA, French B, Aholes AM, Newman AB, Fried LF, Robbins J, et al. Hemoglobin decline, function, and mortality in the elderly: the cardiovascular health study. Am J Hematol 2013;88:5–9.

20. Ludwig H, Strasser K. Symptomatology of anaemia. Semin Oncol 2001;28(2 Suppl. 1):7–14.

21. Eisenstaedt R, Penninx BW, Woodman RC. Anaemia in the elderly: current understanding and emerging concepts. Blood Rev 2006; 20:213–226.

22. Meynard D, Babitt JL, Lin HY. The liver: conductor of systemic iron regulation. Blood 2014;123:168–176.

23. Ferrucci L, Maggio M, Bandinelli S, Basaria S, Lauretani F, Ble A, et al. Low testosterone levels and the risk of anaemia in older men and women. Arch Intern Med 2006;166:1380–1388.

24. Ades L, Itzkyson R, Fenaux P. Myelodysplastic syndromes. Lancet 2014;383:2239–2252.

25. Greenberg PL, Tuechler H, Schanz J, Sanz G, Garcia-Manero G, Solé F, et al. Revised international prognostic scoring system for myelodysplastic syndromes. Blood 2012;120:2454–2465.