Review

Valentina Pecoraro*, Luca Germagnoli and Giuseppe Banfi

Point-of-care testing: where is the evidence? A systematic survey

Abstract: Point-of-care testing (POCT) has had rapid technological development and their use is widespread in clinical laboratories to assure reduction of turn-around-time and rapid patient management in some clinical settings where it is important to make quick decisions. Until now the papers published about the POCT have focused on the reliability of the technology used and their analytical accuracy. We aim to perform a systematic survey of the evidence of POCT efficacy focused on clinical outcomes, selecting POCT denoted special analytes characterized by possible high clinical impact. We searched in Medline and Embase. Two independent reviewers assessed the eligibility, extracted study details and assessed the methodological quality of studies. We analyzed 84 studies for five POCT instruments: neonatal bilirubin, procalcitonin, intra-operative parathyroid hormone, troponin and blood gas analysis. Studies were at high risk of bias. Most of the papers (50%) were studies of correlation between the results obtained by using POCT instruments and those obtained by using laboratory instruments. These data showed a satisfactory correlation between methods when similar analytical reactions were used. Only 13% of the studies evaluated the impact of POCT on clinical practice. POCT decreases the time elapsed for making decisions on patient management but the clinical outcomes have never been adequately evaluated. Our work shows that, although POCT has the potential to provide beneficial patient outcome, further studies may be required, especially for defining its real utility on clinical decision making.

Keywords: clinical decision making; clinical outcome; diagnostic applications; evidence; patient management; point-of-care testing; quality of reporting.

***Corresponding author: Valentina Pecoraro,** Clinical Epidemiologic Unit, IRCCS Galeazzi Orthopedic Institute, Milan, Italy, Phone: +39 02 66214780, Fax: +39 02 66214048, E-mail: valentina.pecoraro@grupposandonato.it
Luca Germagnoli: Unilabs Ticino, Breganzona, Switzerland
Giuseppe Banfi: Clinical Epidemiologic Unit, IRCCS Galeazzi Orthopedic Institute, Milan, Italy; and Department of Biomedical Science for Health, University of Milan, Milan, Italy

Background

Point-of-care testing (POCT) is referred to a near patient, bedside, or extra laboratory testing. It is likely to be carried out by unspecialized staff. By providing results quickly this technology could improve some aspects of laboratory organizations in areas such as emergency rooms, operating rooms and intensive care, but also in mobile vehicles and during transport of patients [1].

A wide number of laboratory tests are now available in different POC devices used for a broad spectrum of diagnostic applications. Several aspects are associated with the rate of POCT implementation [2] such as the reduced complexity of device, type of biological matrices and the high cost, but it is not clear whether the technology has been developed in response to clinical need or whether marketing strategies have led to the perception that this technology is needed. The availability of faster test results should speed diagnosis and treatment, both of which should have a positive impact on patient care. These benefits might also be expected to reduce the amount of time spent by patients waiting in an emergency department and they could reduce the turn-around-time (TAT) of some results, improving patient management [1].

Laboratory professionals more often paid attention to technological aspects of POCT, but there is an increasing interest in its potential clinical outcomes [3]. This emphasis is derived by the need of the adoption of an evidence-based approach for the introduction of new technologies (health technology assessment), and now there is a little evidence that POCT is really improving patient outcomes although rapid supply of results could facilitate clinical decision making [4, 5].

In literature there are many studies comparing POCT and traditional laboratory technologies. Furthermore, organizations and scientific associations have produced a numbers of documents and guidelines to promote the better use of these devices [6, 7]. The purpose of our work is to analyze the scientific literature and identify studies that assess the impact of the POCT on relevant clinical outcomes through a systematic process. The POCT

instruments considered were neonatal bilirubin (Bil), procalcitonin (PCT), parathyroid hormone (PTH), troponin (Tn) and blood gases analyzer (BGa).

Methods

The survey process

The survey was carried out in two steps identified as phases 1 and 2. We applied the systematic methodology suggested by the Cochrane Collaboration to our survey [8].

Phase 1: identification of studies

In phase 1 the assessors have formulated the specific questions about each POCT would be evaluated.

1. Do the measurements of neonatal Bil decrease the number of transfusions and influence the phototherapy practice?
2. Do the measurements of PCT decrease the incidence of major infection and modify the antibiotic therapy?
3. Does the intra-operative PTH assay reduce the number of re-interventions?
4. Does the measurement of Tn decrease the number of myocardial infarctions, mortalities and length of stays (LOSs)?
5. Does BGa in operating and intensive therapy room decrease the incidence of cardiovascular events?

The pathway included four steps: the assessment of the eligibility criteria, the search in major database, the selection of studies and extraction of data. For each type of POCT the authors have searched the studies and extracted major information.

Eligibility criteria

Studies were included if they met the following criteria: 1) Studies randomized, quasi-randomized, prospective or retrospective cohort and case-control; 2) Specimens analyzed by POCT and standard laboratory procedure; 3) Comparison of results between POCT and laboratory instruments; and 4) Report of results of at least one relevant outcome.

The term 'quasi-randomized' refers to controlled trials that use inappropriate randomization strategies [9].

We were very 'inclusive' to reach a pragmatic overall picture of the research status in this field.

Database search for published studies

Studies were identified by searching electronic database and scanning reference lists of articles. This search was applied to Medline (1990–May 2012) and adapted for Embase (1990–May 2012) to capture all potentially relevant English language scientific papers. We considered also the reference list of all potential eligible studies. Databases were searched using the following search terms: point of care testing or point-of-care-testing or POC and troponin or bilirubin or procalcitonin or parathyroid hormone or blood gas analyzer.

Selecting published studies

The literature search was conducted by one investigator (VP). Two researchers (VP or LG) selected independently eligible studies for inclusion. Disagreements between reviewers were resolved by consensus. The abstracts were appraised and publications were selected or rejected based on the inclusion criteria. The full texts of the remaining publications were obtained. Each potentially relevant full text was examined in more detail by all the authors.

Data extraction

Information was extracted from each included studies about: 1) characteristics of study: study design, year, country where the study was performed; 2) characteristics of samples (age, sex, number of sample for each patients, initial and final accrual time); 3) patient important outcome: TAT, LOS, mortality, number of infections, number of re-interventions, recurrence of hyperparathyroidism, major complications; 4) diagnostic accuracy outcomes: sensitivity (Sn), specificity (Sp), likelihood ratio (LR), positive predictive value (PPV), negative predictive value (NPV).

A 'patient important outcome' is an event that has an impact on the patient health status and, when its frequency changes, it becomes of value for the patient [10].

Two authors (VP and LG) independently extracted data from studies and entered in the data extraction form. Disagreements were resolved by discussion.

Phase 2: quality of reporting

In phase 2, the full texts of the included studies were evaluated by two assessors who extracted the relevant information to complete the quality of the reporting checklist.

We moved from the risk of bias tool of the Cochrane Collaboration. As this instrument was created for evaluating randomized controlled trials (RCTs), we slightly adapted it to non-randomized studies (NRS). As reported in the Cochrane Handbook, risk of bias assessment criteria for these trials is not well established [9, 11].

We decided to assess the risk of bias in the following domains: 1) Study designs, i.e., if the study was retrospective or prospective, awarding a low risk of bias to prospective trials; 2) Outcomes reported, i.e., studies including important patient outcomes, as well as LOS and TAT, were evaluated; 3) Blinding, i.e., the outcomes' assessors were blinded, awarding at low risk of bias; 4) Control of known confounding factors at baseline, i.e., samples were selected ad hoc at the beginning of the study, considering at high risk of bias the trials that performed this method.

Every domain could be classified as 'high' or 'low' risk of bias. If the information reported in the paper was not enough, the domain was defined as 'unclear'. Methodological quality was independently assessed by two authors (VP and LG). Disagreements were resolved by consensus.

Results

Study selection

Our literature search identified 456 references: 37 about Bil, 26 about PCT, 10 about PTH, 65 about Tn, and 318 about BGa. Exclusion of duplicates and irrelevant references deleted 99 records. After screening of abstract, 116 studies proved to be eligible for inclusion and their full texts were analyzed in more detail. Thirty-two were excluded because: 1) no comparison with laboratory existed (n=10); 2) did not evaluate POCT (n=10); 3) were narrative review (n=11); and 4) were replaced (n=11). Finally we included 84 studies: 19 Bil [12–30], four PCT [31–34], six PTH [35–40], 25 Tn [41–65], 30 BGa [66–95] (Figure 1).

Study characteristics

The included trials corresponded to seven RCT [46, 49, 50, 52, 57, 62, 83], 56 prospective studies [12–23, 25, 26–30, 31–35, 37–41, 43–45, 47, 48, 51, 53, 55, 56, 58–61, 64–67, 71–74, 76–78, 81, 82, 87, 91], three retrospective [42, 54, 94], one case series [36] and before and after study [63], 16 experimental and cohort studies [24, 68–70, 75, 79, 80, 84–86, 88–90, 92, 93, 95] not better defined. Main features of the studies are summarized in Table 1. Overall, 50,586 sample were considered. Twelve studies were published each from 2010 and 2011, five in the 2009, eight in the 2008, 43 between 2000 and 2007, and 16 before 2000. Thirty-eight studies were published in USA, seven in Germany, six in France, five in the Netherlands and Australia, three in Japan and the UK, two in China, Italy and Switzerland, one each Austria, Belgium, Canada, Denmark, Finland, NC, Singapore, Spain, Sweeden, Taiwan and Turkey.

Seventeen out of 84 studies (20%) reported diagnostic accuracy outcome (Table 1), eight studies about Tn, five studies about Bil, two about PCT and BGa.

Patient important outcomes

There is insufficient evidence that transcutaneous Bil measurement reduces the number of transfusions. No data concerning the possible decrease of transfusion and influence on phototherapy practice exist. Four studies about PCT matched the inclusion criteria and only two reported the number of bacterial infections [32, 33]. No data concerning modification of antibiotic therapy exist. Only one [38] out of six studies about PTH evaluated reduction on TAT and LOS. The study of Chou et al. [36] reported numbers of re-interventions (two patients had a secondary operation) and surgery complications. The majority of studies considered 'important patient outcome' is in the Tn group: eight out of 25 studies (32%) evaluated reduction on LOS, of these seven considered also TAT. Six studies (7%) reported number of patients afflicted by myocardial infarction and four studies (16%) reported data about the mortality. POCT is reported to decrease LOS and TAT about 26 and 56 min, respectively. Studies concerning BGa are experimental studies reporting diagnostic accuracy outcome and did not report data of possible decrease of incidence of cardiovascular events through the use of such a method (Table 2).

Risk of bias within studies

Risk of bias evaluation is reported in Figure 2. Most of studies are prospective so the study design was judged as low risk (green). Many items were judged as unclear (reported in yellow) because the studies did not report enough information for a proper evaluation. In most trials the blinding of outcome assessment was at high risk of bias (red).

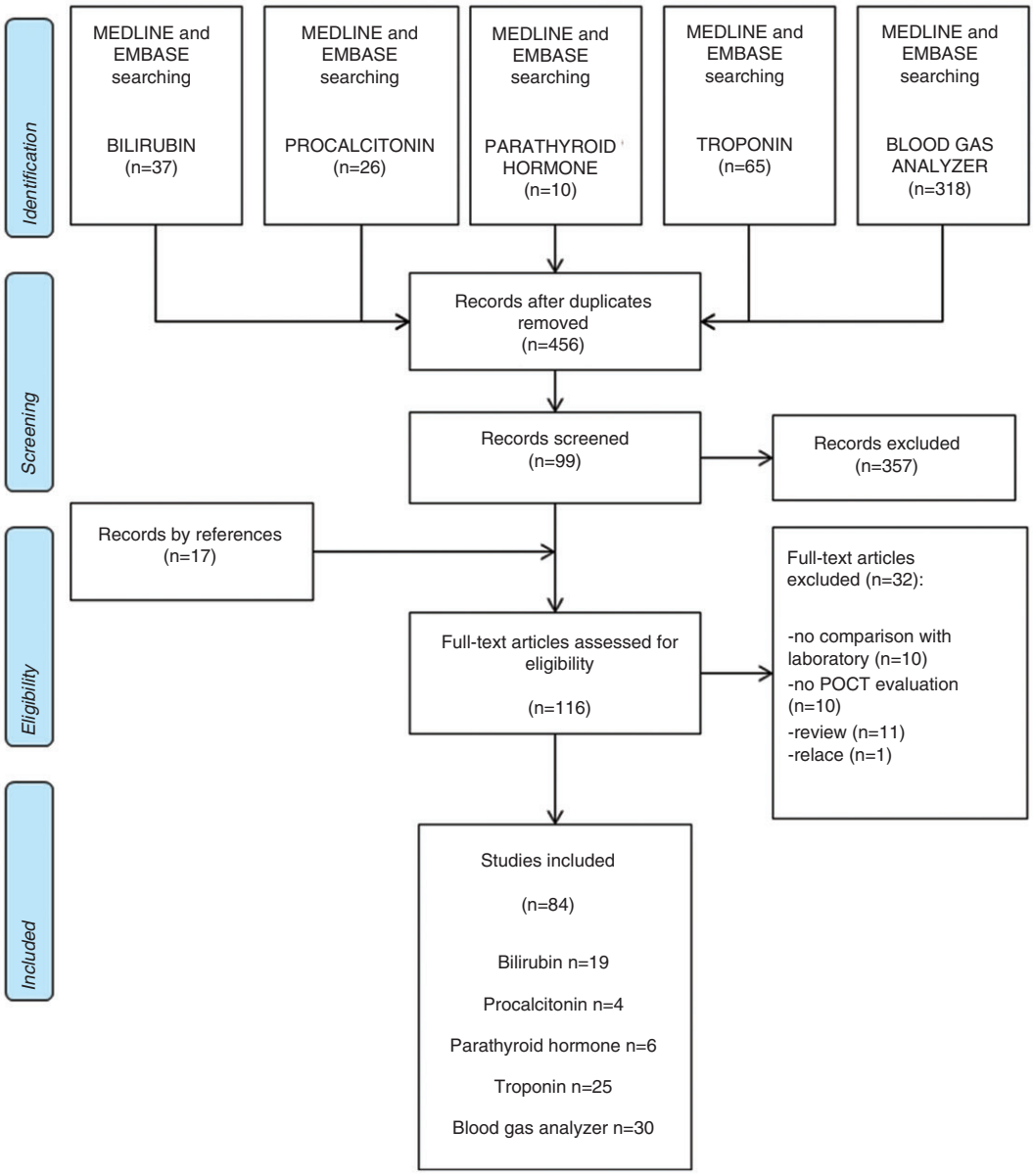


Figure 1 Flow diagram showing the number of record identified, screened, extracted and included in the final analysis.

Discussion

This is the first systematic survey which explores evidence of POCT impact on clinical decision making. We analyzed five POCT instruments measuring neonatal Bil, PCT, PTH, Tn and BGa. The studies evaluated were principally observational studies which correlated laboratory and POCT results. The devices should help the clinical decision making, but only 10 out of 84 studies considered important patient outcomes. The reported quality was generally low; an absence of information about outcome assessment was usual.

The increase of POCT during the last 10 years has been made possible by a number of factors, including advances in computer technology. As POCT methods and instruments require low quantity of biological materials, they are easy to use, smaller and portable, produce results on a variety of analytes more quickly than traditional laboratory instruments, their use appeals to both the medical and nursing or laboratory staff. This advantage does not always mean better patient outcomes, the medical unit that would like to perform POCT should be interested in the real impact of results in clinical practice, besides the accuracy of devices. Kendal et al. [1] have designed

Table 1 Characteristics of studies included.

	Study	Year	Study design	Country	Number of samples	Diagnostic accuracy outcome
Bilirubin	Barko [12]	2006	Prospective	USA	120	SN, SP, PPV, NPV
	Bhutani [13]	2000	Prospective	USA	1788	NR
	Borgard [14]	2006	Prospective	France	473	NR
	Engle [15]	2002	Prospective	USA	404	NR
	Ho [16]	2006	Prospective	China	4689	SN, SP, PPV, NPV
	Kazmierczak [17]	2004	Prospective	USA	Unclear	NR
	Lam [18]	2008	Prospective	China	113	SN, SP
	Maisels [19]	2004	Prospective	USA	849	NR
	Mielsch [20]	2010	Prospective	Germany	240	NR
	Robertson [21]	2002	Prospective	USA	101	NR
	Rolinski [22]	2001	Prospective	Germany	142	NR
	Rubaltelli [23]	2001	Prospective	Italy	NR	NR
	Schmidt [24]	2009	Cohort	USA	94	SN, SP, NPV
	Schumacher [25]	1995	Prospective	USA	NR	NR
	Tan [26]	1996	Prospective	Singapore	540	NR
	Tayaba [27]	1998	Prospective	USA	900	NR
	Wong [28]	2002	Prospective	UK	64	PPV
	Yamanouchi [29]	1980	Prospective	Japan	NR	NR
	Yamauchi [30]	1988	Prospective	Japan	576	NR
Procalcitonin	Bektas [31]	2011	Prospective	Turkey	141	SN, SP, LR+, LR-
	Galetto-Lacour [32]	2003	Prospective	Switzerland	99	SN, SP, PPV, NPV
	Hesselink [33]	2009	Prospective	Netherlands	101	NR
	Meisner [34]	2000	Prospective	Germany	237	NR
PTH	Agarwal [35]	2001	Prospective	Australia	88	NR
	Chou [36]	2002	Case series	Taiwan	NR	NR
	Garner [37]	1999	Prospective	NC	130	NR
	Johnson [38]	2001	Prospective	USA	104	NR
	Mace [39]	2008	Prospective	UK	20	NR
	Sokoll [40]	2000	Prospective	USA	200	NR
Troponin	Apple [41]	2000	Prospective	USA	1550	SN, SP
	Apple [42]	2006	Observational retrospective	USA	545	NR
	Birkhahn [43]	2010	Prospective	USA	151	SN, SP, PPV, NPV
	Bock [44]	2008	Prospective	USA	5909	PPV, NPV
	Caragher [45]	2002	Prospective	USA	205	SN, SP
	Collinson [46]	2004	RCT	UK	163	NR
	Cramer [47]	2007	Prospective	Netherlands	358	NR
	Di Serio [48]	2005	Prospective	Italy	105	NR
	Esposito[49]	2011	Randomized parallel group	USA	2000	NR
	Goodacre [50]	2010	RCT	USA	2263	NR
	Hallani [52]	2005	Randomized	Australia	133	SN, SP, PPV, NPV
	Heeschen [53]	1999	Prospective	USA	412	NR
	Hindle [54]	2005	Retrospective	Canada	235	NR
	Hjortshoj [55]	2011	Prospective	Denmark	458	SN, SP, PPV, NPV
	Lee Lewandrowski [56]	2003	Prospective	USA	369	NR
	Loten [57]	2010	RCT	Australia	912	NR
	Macdonald [58]	2008	Prospective	Australia	100	NR
	McCord [59]	2001	Prospective	USA	1024	SN, SP, NPV
	Muller Bardorff [60]	2000	Prospective	Germany	281	NR
	Ordonez Llanos [61]	2006	Prospective	Spain	1410	NR
	REACTT group [51]	1997	Prospective	USA	721	NR
	Ryan [62]	2009	Randonmized parallel group	USA	2000	NR
	Singer [63]	2008	Before and after	USA	11,266	NR
	Van Domburg [64]	2000	Prospective	Netherlands	1304	NR
	Venge [65]	2010	Prospective	Sweeden	851	SN, SP, PPV, NPV, LR+, LR-

(**Table 1** continued)

	Study	Year	Study design	Country	Number of samples	Diagnostic accuracy outcome
Blood gas	Arora [66]	2011	Prospective	USA	516	SN, SP, PPV, NPV
	Bailey [67]	1998	Prospective	USA	222	NR
	Beneteau Burnat [68]	2004	Experimental	France	20	NR
	Beneteau Burnat [69]	2008	Experimental	France	NR	NR
	Chance [70]	2000	Experimental	USA	NR	NR
	Coplin [71]	1998	Prospective	USA	195	SN, SP
	Dohgomori [72]	2004	Prospective	Japan	27	NR
	Frasca [73]	2011	Prospective	France	471	NR
	Gayat [74]	2001	Prospective	France	200	NR
	Gehring [75]	2002	Experimental	Germany	450	NR
	Grosse [76]	2010	Prospective	Switzerland	NR	NR
	Halpern [77]	1998	Prospective	USA	NR	NR
	Hinkelbein [78]	2008	Prospective	Germany	170	NR
	Jacobs [79]	1993	Experimental	USA	259	NR
	Jain [80]	2009	Cohort	USA	200	NR
	Kilgore [81]	1998	Prospective	USA	NR	NR
	Kulkani [82]	2005	Prospective	Australia	NR	NR
	Leino [83]	2011	RCT	Finland	60	NR
	Lindemans [84]	1999	Experimental	Netherlands	NR	NR
	Ng [85]	2000	Experimental	USA	NR	NR
	Papadea [86]	2002	Experimental	USA	NR	NR
	Petersen [87]	2008	Prospective	USA	114	NR
	Prause [88]	1997	Experimental	Austria	NR	NR
	Schlebush [89]	2001	Experimental	Germany	NR	NR
	Sediame [90]	1999	Experimental	France	92	NR
	Steinfelder Visscher [91]	2006	Prospective	Netherlands	127	NR
	Thomas [92]	2009	Cohort	USA	446	NR
	Walton [93]	2003	Experimental	USA	59	NR
	Wax [94]	2007	Retrospective	USA	NR	NR
	Zaman [95]	2001	experimental	Belgium	20	NR

LR+, positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; NR, not reported; PPV, positive predictive value; PTH, parathyroid hormone SN, sensitivity; SP, specificity.

a randomized controlled trial to assess the accuracy and reproducibility of the results of the test and clinical outcome. They reported that POCT produced a time critical benefit for 7% patients and POCT influenced treatment in 14% of cases overall. Also, there were no difference in the amount of time spent in the emergency department, LOS and mortality. They concluded that POCT results would result in a clinical important reduction in the time elapsed in clinical differential diagnosis and treatment decision, but the methodology of studies should be improved.

The role of the POCT concerns the help in making clinical decisions. Several studies have investigated the

Table 2 Number of studies reporting data about important patients' outcome.

	n	TAT	LOS	Mortality	Several bacterial infection	Number of re-intervention	Recurrence of hyperparathyroidism	Major complication
Bilirubin	19	1	0	0	–	–	–	–
PCT	4	0	0	0	2	–	–	0
PTH	6	1	1	0	–	1	1	1
Tn	25	7	8	4	–	–	–	0
BGa	30	1	0	0	–	–	–	0
TOT	84	10	9	4	2	1	1	1

BGa, blood gas analyzer; LOS, lost to follow-up; PCT, procalcitonin; PTH, parathyroid hormone; TAT, turn-around-time; TN, troponin.
n, number of studies included in each group of POC.

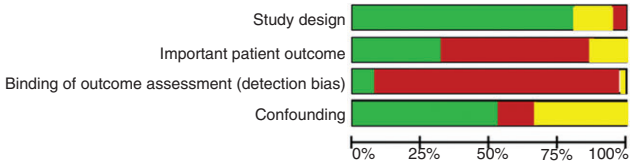


Figure 2 Risk of bias.
Red, high risk of bias; yellow, unknown risk of bias; green, low risk of bias.

implementation of these POCT devices in a clinical setting. Altinier et al. [96] evaluated POCT for cardiac markers in the emergency department. POCT can reduce TAT and allow rapid provision of results. However, there are not RCTs to determine whether the devices can change patient management and reduce hospital admission. POCT are often used for self-monitoring of oral anticoagulation and its use leads to a significant reduction in death but also in major clinical events. The study of Ryan et al. [62] explored if POCT decreases the LOS of patients in emergency department. The authors conclude that POCT had the potential to reduce time in decision making, in fact POCT decreases the proportion of test results available to the physician within 30 or 60 min. The results demonstrated variable benefits of POCT and, when benefits were evident, they were not as extensive as it might be assumed from the concept that rapid results are translated into a rapid decision.

We evaluated biochemical tests which are common in clinical practice, but POCT are not implemented routinely for these tests, with the exception of blood gas. The most common test for which POCT is available is the measurement of glycated hemoglobin, employed in monitoring of diabetes patients. Although the test is used daily in clinical setting, a recent systematic review of Al-Ansary et al. [97] concluded that there is not enough evidence of the effectiveness of POCT for glycated hemoglobin due to some limitations of the studies design. Similarly, new technologies were implemented to simplify parathyroidectomy surgery. Previews studies have clearly shown that this approach leads to successful clinical outcomes and some suggest that it can lead to decrease costs through less exposure to anesthesia and shorter hospital stays [38]. Our survey, instead, included six studies about PTH and only one (Chou [36]) reported the number of re-interventions.

Overall, there are different opinions regarding the issue of POCT implementation. Several studies support POCT as an alternative to laboratory [61, 98] reporting good concordance such as Bil, while others find little discrepancies in comparisons [47].

Although there is an improvement of patient management when using POCT, there are not RCTs concerning the relationship between physician decision and patient improvement. Our results show that only 13% of studies evaluated important outcome and the measures were not assessed masked. It is not always possible to blind physician and patients because the clinical decision is made at the time the result is produced. However, blinded measurement and reporting of outcome are possible.

Most of the published studies evaluated measurements in the clinical pathway which are surrogate outcomes. Surrogate outcomes are outcomes for which changes do not directly impact the patient's disease status or well being, but which are theoretically tied to the patient's disease process management [10]. Surrogate markers include changes in laboratory parameters (e.g., cholesterol levels as a surrogate for myocardial infarction). Authors may be tempted to use surrogate endpoints because they usually occur more frequently than patient important outcomes. Use of surrogate markers requires complete confidence that each outcome correlates consistently with a patient important outcome (i.e., survival) [10]. Sometimes the surrogated outcome may not be casually or strongly related to the clinical outcome, but it can be only a concomitant factor, and thus it may not predict the effect on the clinical outcome [99]. La Cour et al. [100] reported that one in five randomized controlled trials used surrogate outcomes as a primary outcome and highlight that a correct report and evaluation of surrogate outcomes is needed.

We observed some noise in the use of these devices, emphasizing the additional issue that should be addressed in future studies: 1) there is insufficient evidence of the effectiveness of POCT in clinical decision making; 2) the current literature requires further development; and 3) economic analysis exploring whether the potential benefit of POCT justifies the additional cost is needed.

Our findings suggest that POCT may be clinically beneficial for some presenting complaints. Further studies are required for investigating the economic and clinical benefits of POCT and these studies are crucial for the definition of the efficacy of POCT in the clinical setting. However, even trials based on validated surrogate outcomes may not be able to capture unexpected important harmful effects of the implementations of technology.

Our results are in line with the National Academy of Clinical Biochemistry Laboratory Medicine Practice Guideline [7]. The document offers recommendation to improve the analytical performance and clinical utility of POCT by reporting the evidence about some instruments. Authors reported evidence about the major POCT used in clinical practice and highlighted the limited available evidence for some of these (i.e., Bil) and concluded the need to provide a better link between POCT and patient outcome.

We studied literature concerning POCT which have possibly real impact on clinical decisions, especially for emergency department (Tn, BGa, PCT), surgery (PTH), and internal medicine (Bil). Surprisingly, we did not find specific literature based on RCTs and cost-effectiveness studies, even for very common POCT devices, as glucometers or urine analyzers.

Moreover, the wide acceptance of common marketing appeal for POCT devices, particularly for the tests we studied, is not really evidenced by published studies, although in some cases, e.g., BGa, their number is very high. A complete redefinition of aims and methodology of studies devoted to POCT should be acknowledged.

A careful appraisal of the impact of its use in clinical practice should be carried out. Randomized controlled trials are needed to investigate the impact of the test on patient management and outcomes.

Acknowledgments: All authors contributed to the execution of the review. VP and LG conceived the study. VP and LG wrote the protocol. VP designed and implemented the search strategies. VP and LG selected studies, assessed validity, extracted data and assessed the quality of reporting. GB was consulted where necessary. VP entered and analyzed the data. VP, LG and GB prepared the full review. All authors contributed to its revision, interpretation of results, and approval.

Conflict of interest statement

Authors' conflict of interest disclosure: The authors stated that there are no conflicts of interest regarding the publication of this article.
Research funding: None declared.
Employment or leadership: None declared.
Honorarium: None declared.

Received May 22, 2013; accepted July 26, 2013

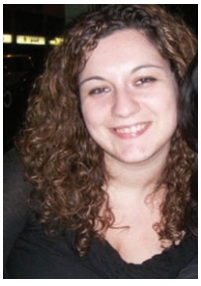
References

1. Kendall J, Reeves B, Clancy M. Point of care testing: randomised controlled trial of clinical outcome. Br Med J 1998;316:1052–7.
2. Fleisher M. Point-of-care testing: does it really improve patient care. Clin Biochem 1993;26:6–8.
3. Price CP, St John A, Kricka LJ. Putting point-of-care testing into context: moving beyond innovation to adoption. In: Price CP, St John A, Kricka LR, editors. Point-of-care testing, 3rd ed. Washington DC: AACC Press, 2010:1–20.
4. St John A. The evidence to support point-of-care testing. Clin Biochem Rev 2010;31:111–9.
5. Price CP. Point of care testing. Br Med J 2001;322:1285–8.
6. Briedigkeit L, Muller-Plathe O, Schlebusch H, Ziems J. Recommendations of the German working group on medical laboratory testing (AML) on the introduction and quality assurance of procedures for point-of-care testing (POCT) in hospitals. Clin Chem Lab Med 1999;37:919–25.
7. Nichols JH, Christenson RH, Clarke W, Gronowski A, Hammett-Stabler CA, Jacobs E, et al. Executive summary. The national academy of clinical biochemistry laboratory medicine practice guideline: evidence-based practice for point-of-care testing. Clin Chim Acta 2007;379:14–28.
8. Higgins JP, Green S, editors. Cochrane handbook for systematic reviews of interventions. John Wiley & Sons Ltd, 2011.
9. Reeves BC, Deeks JJ, Higgins JP, Wells GA. Including non-randomized studies. In: Higgins JP, Green S, editors. Cochrane handbook for systematic reviews of interventions. Chichester, West Sussex: John Wiley & Sons Ltd, 2011.
10. Crowther MA. Introduction to surrogates and evidence-based mini-reviews. Hematology Am Soc Hematol Educ Program 2009:15–6.
11. Higgins JP, Altman DG. Assessing risk of bias in included studies. In: Higgins JP, Green S, editors. Cochrane handbook for systematic reviews of interventions. Chichester, West Sussex: John Wiley & Sons Ltd, 2008.
12. Barko HA, Jackson GL, Engle WD. Evaluation of a point-of-care direct spectrophotometric method for measurement of total serum bilirubin in term and near-term neonates. J Perinatol 2006;26:100–5.
13. Bhutani VK, Gourley GR, Adler S, Kreamer B, Dalin C, Johnson LH. Noninvasive measurement of total serum bilirubin in a multiracial predischarge newborn population to assess the risk of severe hyperbilirubinemia. Pediatrics 2000;106:E17.
14. Borgard JP, Szymanowicz A, Pellae I, Szmidt-Adjide V, Rota M. Determination of total bilirubin in whole blood from neonates: results from a French multicenter study. Clin Chem Lab Med 2006;44:1103–10.
15. Engle WD, Jackson GL, Sendelbach D, Manning D, Frawley WH. Assessment of a transcutaneous device in the evaluation of neonatal hyperbilirubinemia in a primarily Hispanic population. Pediatrics 2002;110:61–7.
16. Ho HT, Ng TK, Tsui KC, Lo YC. Evaluation of a new transcutaneous bilirubinometer in Chinese newborns. Arch Dis Child Fetal Neonatal Ed 2006;91:F434–8.
17. Kazmierczak SC, Robertson AF, Briley KP, Kreamer B, Gourley GR. Transcutaneous measurement of bilirubin in newborns: comparison with an automated Jendrassik-Grof procedure and HPLC. Clin Chem 2004;50:433–5.
18. Lam TS, Tsui KL, Kam CW. Evaluation of a point-of-care transcutaneous bilirubinometer in Chinese neonates at an accident and emergency department. Hong Kong Med J 2008;14:356–60.

19. Maisels MJ, Ostrea EM, Jr., Touch S, Clune SE, Cepeda E, Kring E, et al. Evaluation of a new transcutaneous bilirubinometer. Pediatrics 2004;113:1628–35.
20. Mielsch C, Zimmermann A, Wagner D, Matthes B, Schlebusch H, Luppa PB. Point-of-care determination of neonatal bilirubin with the blood gas analyzer RapidLab 1265. Clin Chem Lab Med 2010;48:1455–61.
21. Robertson A, Kazmierczak S, Vos P. Improved transcutaneous bilirubinometry: comparison of SpectR(X) BiliCheck and Minolta jaundice meter JM-102 for estimating total serum bilirubin in a normal newborn population. J Perinatol 2002;22:12–4.
22. Rolinski B, Kuster H, Ugele B, Gruber R, Horn K. Total bilirubin measurement by photometry on a blood gas analyzer: potential for use in neonatal testing at the point of care. Clin Chem 2001;47:1845–7.
23. Rubaltelli FF, Gourley GR, Loskamp N, Modi N, Roth-Kleiner M, Sender A, et al. Transcutaneous bilirubin measurement: a multicenter evaluation of a new device. Pediatrics 2001;107:1264–71.
24. Schmidt ET, Wheeler CA, Jackson GL, Engle WD. Evaluation of transcutaneous bilirubinometry in preterm neonates. J Perinatol 2009;29:564–9.
25. Schumacher RE, Thornbery JM, Gutcher GR. Transcutaneous bilirubinometry: a comparison of old and new methods. Pediatrics 1985;76:10–4.
26. Tan KL, Chia HP, Koh BC. Transcutaneous bilirubinometry in Chinese, Malay and Indian infants. Acta Paediatr 1996;85: 986–90.
27. Tayaba R, Gribetz D, Gribetz I, Holzman IR. Noninvasive estimation of serum bilirubin. Pediatrics 1998;102:E28.
28. Wong CM, van Dijk PJ, Laing IA. A comparison of transcutaneous bilirubinometers: SpectRx BiliCheck versus Minolta AirShields. Arch Dis Child Fetal Neonatal Ed 2002;87:F137–40.
29. Yamanouchi I, Yamauchi Y, Igarashi I. Transcutaneous bilirubinometry: preliminary studies of noninvasive transcutaneous bilirubin meter in the Okayama National Hospital. Pediatrics 1980;65:195–202.
30. Yamauchi Y, Yamanouchi I. Transcutaneous bilirubinometry. Evaluation of accuracy and reliability in a large population. Acta Paediatr Scand 1988;77:791–5.
31. Bektas F, Soyuncu S, Gunduz I, Basarici I, Akbas H, Eken C. The value of procalcitonin, a novel inflammatory marker, in the diagnosis of myocardial infarction and evaluation of acute coronary syndrome patients. J Emerg Med 2011;41:524–30.
32. Galetto-Lacour A, Zamora SA, Gervaix A. Bedside procalcitonin and C-reactive protein tests in children with fever without localizing signs of infection seen in a referral center. Pediatrics 2003;112:1054–60.
33. Hesselink DA, Burgerhart JS, Bosmans-Timmerarends H, Petit P, van Genderen PJ. Procalcitonin as a biomarker for severe Plasmodium falciparum disease: a critical appraisal of a semi-quantitative point-of-care test in a cohort of travellers with imported malaria. Malar J 2009;8:206.
34. Meisner M, Brunkhorst FM, Reith HB, Schmidt J, Lestin HG, Reinhart K. Clinical experiences with a new semi-quantitative solid phase immunoassay for rapid measurement of procalcitonin. Clin Chem Lab Med 2000;38:989–95.
35. Agarwal G, Barakate MS, Robinson B, Wilkinson M, Barraclough B, Reeve TS, et al. Intraoperative quick parathyroid hormone versus same-day parathyroid hormone testing for minimally invasive parathyroidectomy: a cost-effectiveness study. Surgery 2001;130:963–70.
36. Chou FF, Lee CH, Chen JB, Hsu KT, Sheen-Chen SM. Intraoperative parathyroid hormone measurement in patients with secondary hyperparathyroidism. Arch Surg 2002;137:341–4.
37. Garner SC, Leight GS, Jr. Initial experience with intraoperative PTH determinations in the surgical management of 130 consecutive cases of primary hyperparathyroidism. Surgery 1999;126:1132–7.
38. Johnson LR, Doherty G, Lairmore T, Moley JF, Brunt LM, Koenig J, et al. Evaluation of the performance and clinical impact of a rapid intraoperative parathyroid hormone assay in conjunction with preoperative imaging and concise parathyroidectomy. Clin Chem 2001;47:919–25.
39. Mace AD, Randhawa PS, Woolman E, Stearns MP. Intra-operative parathyroid hormone monitoring using a laboratory based multichannel analyser. Clin Otolaryngol 2008;33:134–7.
40. Sokoll LJ, Drew H, Udelsman R. Intraoperative parathyroid hormone analysis: a study of 200 consecutive cases. Clin Chem 2000;46:1662–8.
41. Apple FS, Anderson FP, Collinson P, Jesse RL, Kontos MC, Levitt MA, et al. Clinical evaluation of the first medical whole blood, point-of-care testing device for detection of myocardial infarction. Clin Chem 2000;46:1604–9.
42. Apple FS, Chung AY, Kogut ME, Bubany S, Murakami MM. Decreased patient charges following implementation of point-of-care cardiac troponin monitoring in acute coronary syndrome patients in a community hospital cardiology unit. Clin Chim Acta 2006;370:191–5.
43. Birkhahn RH, Haines E, Wen W, Reddy L, Briggs WM, Datillo PA. Estimating the clinical impact of bringing a multimarker cardiac panel to the bedside in the ED. Am J Emerg Med 2010;29:304–8.
44. Bock JL, Singer AJ, Thode HC, Jr. Comparison of emergency department patient classification by point-of-care and central laboratory methods for cardiac troponin I. Am J Clin Pathol 2008;130:132–5.
45. Caragher TE, Fernandez BB, Jacobs FL, Barr LA. Evaluation of quantitative cardiac biomarker point-of-care testing in the emergency department. J Emerg Med 2002;22:1–7.
46. Collinson PO, John C, Lynch S, Rao A, Canepa-Anson R, Carson E, et al. A prospective randomized controlled trial of point-of-care testing on the coronary care unit. Ann Clin Biochem 2004;41:397–404.
47. Cramer GE, Kievit PC, Brouwer MA, de Keijzer MH, Luijten HE, Verheugt FW. Lack of concordance between a rapid bedside and conventional laboratory method of cardiac troponin testing: impact on risk stratification of patients suspected of acute coronary syndrome. Clin Chim Acta 2007;381:164–6.
48. Di Serio F, Amodio G, Varraso L, Campaniello M, Coluccia P, Trerotoli P, et al. Integration between point-of-care cardiac markers in an emergency/cardiology department and the central laboratory: methodological and preliminary clinical evaluation. Clin Chem Lab Med 2005;43:202–9.
49. Esposito EC, Hollander JE, Ryan RJ, Schreiber D, O'Neil B, Jackson R, et al. Predictors of 30-day cardiovascular events in patients with prior percutaneous coronary intervention or coronary artery bypass grafting. Acad Emerg Med 2011;18:613–8.
50. Goodacre SW, Bradburn M, Cross E, Collinson P, Gray A, Hall AS. The randomised assessment of treatment using panel assay of

cardiac markers (RATPAC) trial: a randomised controlled trial of point-of-care cardiac markers in the emergency department. Heart 2011;97:190–6.
51. Group RS. Evaluation of a bedside whole-blood rapid troponin T assay in the emergency department. Rapid evaluation by assay of cardiac troponin T (REACTT) investigators study group. Acad Emerg Med 1997;4:1018–24.
52. Hallani H, Leung DY, Newland E, Juergens CP. Use of a quantitative point-of-care test for the detection of serum cardiac troponin T in patients with suspected acute coronary syndromes. Intern Med J 2005;35:560–2.
53. Heeschen C, Goldmann BU, Moeller RH, Hamm CW. Analytical performance and clinical application of a new rapid bedside assay for the detection of serum cardiac troponin I. Clin Chem 1998;44:1925–30.
54. Hindle HR, Hindle SK. Qualitative troponin I estimation in the diagnosis of acute coronary syndromes in three rural hospitals. Can J Rural Med 2005;10:225–30.
55. Hjortshoj S, Venge P, Ravkilde J. Clinical performance of a new point-of-care cardiac troponin I assay compared to three laboratory troponin assays. Clin Chim Acta 2011;412:370–5.
56. Lee-Lewandrowski E, Corboy D, Lewandrowski K, Sinclair J, McDermot S, Benzer TI. Implementation of a point-of-care satellite laboratory in the emergency department of an academic medical center. Impact on test turnaround time and patient emergency department length of stay. Arch Pathol Lab Med 2003;127:456–60.
57. Loten C, Attia J, Hullick C, Marley J, McElduff P. Point of care troponin decreases time in the emergency department for patients with possible acute coronary syndrome: a randomised controlled trial. Emerg Med J 2010;27:194–8.
58. Macdonald SP, Nagree Y. Rapid risk stratification in suspected acute coronary syndrome using serial multiple cardiac biomarkers: a pilot study. Emerg Med Australas 2008;20:403–9.
59. McCord J, Nowak RM, McCullough PA, Foreback C, Borzak S, Tokarski G, et al. Ninety-minute exclusion of acute myocardial infarction by use of quantitative point-of-care testing of myoglobin and troponin I. Circulation 2001;104:1483–8.
60. Muller-Bardorff M, Sylven C, Rasmanis G, Jorgensen B, Collinson PO, Waldenhofer U, et al. Evaluation of a point-of-care system for quantitative determination of troponin T and myoglobin. Clin Chem Lab Med 2000;38:567–74.
61. Ordonez-Llanos J, Santalo-Bel M, Merce-Muntanola J, Collinson PO, Gaze D, Haass M, et al. Risk stratification of chest pain patients by point-of-care cardiac troponin T and myoglobin measured in the emergency department. Clin Chim Acta 2006;365:93–7.
62. Ryan RJ, Lindsell CJ, Hollander JE, O'Neil B, Jackson R, Schreiber D, et al. A multicenter randomized controlled trial comparing central laboratory and point-of-care cardiac marker testing strategies: the disposition impacted by serial point of care markers in acute coronary syndromes (DISPO-ACS) trial. Ann Emerg Med 2009;53:321–8.
63. Singer AJ, Viccellio P, Thode HC, Jr., Bock JL, Henry MC. Introduction of a stat laboratory reduces emergency department length of stay. Acad Emerg Med 2008;15:324–8.
64. van Domburg RT, Cobbaert C, Kimman GJ, Zerback R, Simoons ML. Long-term prognostic value of serial troponin T bedside tests in patients with acute coronary syndromes. Am J Cardiol 2000;86:623–7.
65. Venge P, Ohberg C, Flodin M, Lindahl B. Early and late outcome prediction of death in the emergency room setting by point-of-care and laboratory assays of cardiac troponin I. Am Heart J 2010;160:835–41.
66. Arora S, Henderson SO, Long T, Menchine M. Diagnostic accuracy of point-of-care testing for diabetic ketoacidosis at emergency-department triage: {beta}-hydroxybutyrate versus the urine dipstick. Diabetes Care 2011;34:852–4.
67. Bailey PL, McJames SW, Cluff ML, Wells DT, Orr JA, Westenskow DR, et al. Evaluation in volunteers of the VIA V-ABG automated bedside blood gas, chemistry, and hematocrit monitor. J Clin Monit Comput 1998;14:339–46.
68. Beneteau-Burnat B, Bocque MC, Lorin A, Martin C, Vaubourdolle M. Evaluation of the blood gas analyzer Gem PREMIER 3000. Clin Chem Lab Med 2004;42:96–101.
69. Beneteau-Burnat B, Pernet P, Pilon A, Latour D, Goujon S, Feuillu A, et al. Evaluation of the GEM premier 4000: a compact blood gas CO-Oximeter and electrolyte analyzer for point-of-care and laboratory testing. Clin Chem Lab Med 2008;46:271–9.
70. Chance JJ, Li DJ, Sokoll LJ, Silberman MA, Engelstad ME, Nichols JH, et al. Multiple site analytical evaluation of a portable blood gas/electrolyte analyzer for point of care testing. Crit Care Med 2000;28:2081–5.
71. Coplin WM, O'Keefe GE, Grady MS, Grant GA, March KS, Winn HR, et al. Accuracy of continuous jugular bulb oximetry in the intensive care unit. Neurosurgery 1998;42:533–9.
72. Dohgomori H, Arikawa K, Kanmura Y. Accuracy of a point-of-care blood gas analyzer in gastric tonometry measurements of intramucosal pH (pHi) and P(CO2) gap. J Anesth 2004; 18:14–7.
73. Frasca D, Dahyot-Fizelier C, Catherine K, Levrat Q, Debaene B, Mimoz O. Accuracy of a continuous noninvasive hemoglobin monitor in intensive care unit patients. Crit Care Med 2011;39:2277–82.
74. Gayat E, Bodin A, Sportiello C, Boisson M, Dreyfus JF, Mathieu E, et al. Performance evaluation of a noninvasive hemoglobin monitoring device. Ann Emerg Med 2011;57:330–3.
75. Gehring H, Hornberger C, Dibbelt L, Rothsigkeit A, Gerlach K, Schumacher J, et al. Accuracy of point-of-care-testing (POCT) for determining hemoglobin concentrations. Acta Anaesthesiol Scand 2002;46:980–6.
76. Grosse FO, Holzhey D, Falk V, Schaarschmidt J, Kraemer K, Mohr FW. In vitro comparison of the new in-line monitor BMU 40 versus a conventional laboratory analyzer. J Extra Corpor Technol 2010;42:61–70.
77. Halpern MT, Palmer CS, Simpson KN, Chesley FD, Luce BR, Suyderhoud JP, et al. The economic and clinical efficiency of point-of-care testing for critically ill patients: a decision-analysis model. Am J Med Qual 1998;13:3–12.
78. Hinkelbein J, Floss F, Denz C, Krieter H. Accuracy and precision of three different methods to determine Pco2 (Paco2 vs. Petco2 vs. Ptcco2) during interhospital ground transport of critically ill and ventilated adults. J Trauma 2008;65:10–8.
79. Jacobs E, Nowakowski M, Colman N. Performance of Gem premier blood gas/electrolyte analyzer evaluated. Clin Chem 1993;39:1890–3.
80. Jain A, Subhan I, Joshi M. Comparison of the point-of-care blood gas analyzer versus the laboratory auto-analyzer for the measurement of electrolytes. Int J Emerg Med 2009;2:117–20.

81. Kilgore ML, Steindel SJ, Smith JA. Evaluating stat testing options in an academic health center: therapeutic turnaround time and staff satisfaction. Clin Chem 1998;44:1597–603.
82. Kulkarni A, Saxena M, Price G, O'Leary MJ, Jacques T, Myburgh JA. Analysis of blood glucose measurements using capillary and arterial blood samples in intensive care patients. Intensive Care Med 2005;31:142–5.
83. Leino A, Kurvinen K. Interchangeability of blood gas, electrolyte and metabolite results measured with point-of-care, blood gas and core laboratory analyzers. Clin Chem Lab Med 2011;49:1187–91.
84. Lindemans J, Hoefkens P, van Kessel AL, Bonnay M, Kulpmann WR, van Suijlen JD. Portable blood gas and electrolyte analyzer evaluated in a multiinstitutional study. Clin Chem 1999;45:111–7.
85. Ng IO, Liu CL, Fan ST, Ng M. Expression of P-glycoprotein in hepatocellular carcinoma. A determinant of chemotherapy response. Am J Clin Pathol 2000;113:355–63.
86. Papadea C, Foster J, Grant S, Ballard SA, Cate JC, Southgate WM, et al. Evaluation of the i-STAT portable clinical analyzer for point-of-care blood testing in the intensive care units of a university children's hospital. Ann Clin Lab Sci 2002;32:231–43.
87. Petersen JR, Graves DF, Tacker DH, Okorodudu AO, Mohammad AA, Cardenas VJ, Jr. Comparison of POCT and central laboratory blood glucose results using arterial, capillary, and venous samples from MICU patients on a tight glycemic protocol. Clin Chim Acta 2008;396:10–3.
88. Prause G, Ratzenhofer-Komenda B, Offner A, Lauda P, Voit H, Pojer H. Prehospital point of care testing of blood gases and electrolytes – an evaluation of IRMA. Crit Care 1997;1: 79–83.
89. Schlebusch H, Paffenholz I, Zerback R, Leinberger R. Analytical performance of a portable critical care blood gas analyzer. Clin Chim Acta 2001;307:107–12.
90. Sediame S, Zerah-Lancner F, d'Ortho MP, Adnot S, Harf A. Accuracy of the i-STAT bedside blood gas analyser. Eur Respir J 1999;14:214–7.
91. Steinfelder-Visscher J, Weerwind PW, Teerenstra S, Brouwer MH. Reliability of point-of-care hematocrit, blood gas, electrolyte, lactate and glucose measurement during cardio-pulmonary bypass. Perfusion 2006;21:33–7.
92. Thomas FO, Hoffman TL, Handrahan DL, Crapo RO, Snow G. The measure of treatment agreement between portable and laboratory blood gas measurements in guiding protocol-driven ventilator management. J Trauma 2009;67:303–13.
93. Walton HG, Boucher DM, Marroquin R. Comparison of blood gas and electrolyte test results from the Gem-premier and the ABL-70 versus a conventional laboratory analyzer. J Extra Corpor Technol 2003;35:24–7.
94. Wax DB, Reich DL. Changes in utilization of intraoperative laboratory testing associated with the introduction of point-of-care testing devices in an academic department. Anesth Analg 2007;105:1711–3.
95. Zaman Z, Demedts M. Blood gas analysis: POCT versus central laboratory on samples sent by a pneumatic tube system. Clin Chim Acta 2001;307:101–6.
96. Altinier S, Zaninotto M, Mion M, Carraro P, Rocco S, Tosato F, et al. Point-of-care testing of cardiac markers: results from an experience in an emergency department. Clin Chim Acta 2001;311:67–72.
97. Al-Ansary L, Farmer A, Hirst J, Roberts N, Glasziou P, Perera R, et al. Point-of-care testing for Hb A1c in the management of diabetes: a systematic review and metaanalysis. Clin Chem 2011;57:568–76.
98. Wu AH, Smith A, Christenson RH, Murakami MM, Apple FS. Evaluation of a point-of-care assay for cardiac markers for patients suspected of acute myocardial infarction. Clin Chim Acta 2004;346:211–9.
99. Gotzsche PC, Liberati A, Torri V, Rossetti L. Beware of surrogate outcome measures. Int J Technol Assess Health Care 1996;12:238–46.
100. la Cour JL, Brok J, Gotzsche PC. Inconsistent reporting of surrogate outcomes in randomised clinical trials: cohort study. Br Med J 2010;341:c3653.



Valentina Pecoraro graduated in Biology at University of Perugia. After receiving her degree she started to work in the Italian Cochrane Centre, Mario Negri Institute for Pharmacological Research in Milan. She refined her professional activities by participating at an advanced course in systematic reviews and meta-analysis. Presently Valentina is a researcher of Clinical Epidemiology Unit at IRCCS Galeazzi. Her scientific areas of interest are: the methodology of diagnostic and efficacy systematic reviews, valuation of methodological quality of primary studies and systematic reviews, elaboration of literature search strategy. She is attending a postgraduate school in Clinical Biochemistry and Clinical Molecular Biology at University of Milan.

Luca Germagnoli received his postgraduates in haematology and clinical chemistry at the University of Milan, Italy. He worked until 2008 in San Raffaele hospital laboratory, Milan (Laboraf) and his main interests were in the design and implementation of automation systems for the clinical laboratory and in the realization and remote control of networks of POC analyzers. Since September 2008 to the present time he is scientific director and chief of the haematology-clinical chemistry area and of the proximity laboratories in Unilabs Ticino laboratory, a large private clinical laboratory in Lugano, Switzerland. He is currently involved in evidence-based medicine projects related to topics of clinical and laboratory medicine.

Giuseppe Banfi graduated in Medicine in 1984 at Università di Pavia. In 1988 he postgraduated in Hygiene and Preventive Medicine at the University of Milano (Italy). He started his career working in the analysis laboratory in San Raffaele hospital as assistant from 1985 to 1991. From 1991 to 1997 he became deputy director of the analysis laboratory of the Scientific Institute San Raffaele. In 1997 he moved to S. Maria Clinic (Castellanza) as medical superintendent. He moved to the Institute Villa Aprica (Como) as Medical Superintendent (2001–2003). From February 2003 to September 2008 he was Medical Superintendent of the Orthopedic Institute Galeazzi in Milan. From May 2007 he was engaged also as Scientific Director and Director of Research programs of Scientific Institute Galeazzi. Associate Professor of Clinical Biochemistry and Clinical Molecular Biology at School of Medicine, University of Milan. Giuseppe is the author of 180 papers published in peer-reviewed journals.