Contents lists available at ScienceDirect

EBioMedicine

journal homepage: www.ebiomedicine.com

How Long can we Store Blood Samples: A Systematic Review and Meta-Analysis

Dong-wen Wu*, Yu-meng Li, Fen Wang

Third Xiangya Hospital, Central South University, Changsha, China

ARTICLE INFO

Article history: Received 7 August 2017 Received in revised form 11 September 2017 Accepted 18 September 2017 Available online 23 September 2017

Keywords: Blood sample storage Complete blood count (CBC) Comprehensive metabolic panel (CMP) testing Meta-analysis

ABSTRACT

Objective: To assess the effect of storage time and temperature on complete blood count (CBC) and comprehensive metabolic panel (CMP) testing.

Methods: PubMed, EMBASE, the Cochrane Library of Systematic Reviews, Web of Science (WOS), China National Knowledge Infrastructure (CNKI), WanFang databases and SinoMed databases were searched up to May 2017. Clinical trials with adult whole blood samples were identified. Paired reviewers independently screened, extracted data and evaluated the quality of evidence (MINORS tool). Analyses were conducted using Revman 5.3 and Stata 14.0.

Results: A total of 89 studies were confirmed. For CBC, except MPV, most parameters were stable at least for 24 h. Some indices, such as WBC, PLt, HCT, HGB and MCH were stable up to 3 d. However, stable CMP test results could only be acquired within 12 h. at 4 °C, including GLU, AST, ALT, Na, ALB, Cl, DBIL, TC, TG and ALP. Values were less stable when stored at RT.

Conclusions: Specimens stored >12 h. for CMP may generate unreliable results. For CBC, samples could reliably be stored for 24 h. For longer storage, refrigeration (at 4 °C) would be a better choice.

© 2017 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Delayed sample analysis for organizational, technical reasons or questionable results that need to be verified are not rare in clinical practice (Lippi and Simundic, 2012). Besides, the reorganization of laboratory services around the globe entails the consolidation of small laboratories into larger facilities in the era of new public health initiatives. A large number of specimens are dispatched from peripheral centers to a centralized laboratory over long distances where a delay of 12– 24 h or more occurred. Moreover, at weekends, this interval may exceed 36 h due to closure of the laboratory (Lippi and Simundic, 2012). The significant delay and poor storage specimens could lead to imprecise, inaccurate and unreliable results (Briggs et al., 2014; Imeri et al., 2008; Zini, 2014) which adversely affect clinical decisions ultimately (Zandecki et al., 2007).

Complete blood count (CBC) and comprehensive metabolic panel (CMP) testing are the most routinely done laboratory tests giving basic and valuable information not only in facilitating the diagnosis and directing further testing but also in monitoring the patient(Plebani and Lippi, 2010). This is especially true for those who need transfusion.

* Corresponding author at: Tongzipo Road 138#, Yuelu District, Changsha 410010, Hunan Province, China.

E-mail address: 2204120613@csu.edu.cn (D. Wu).

Since blood tests are commoner than testing other biological fluids, it is important to determine the suitable temperature and duration of storage (Mosca et al., 2009). Various articles focusing on this have been published, but results are often contradictory which could be a result of differences in sample sizes and other factors, such as the different analyzers. Unfortunately, evidence-based confirmation by large-scale clinical trials is still lacking. Therefore, we conducted this meta-analysis to quantitatively inspect the influence of storage time and temperature on CBC and CMP testing.

2. Materials and Methods

This review is reported according to Preferred Reporting Items for Systematic Reviews statement for reporting systematic reviews and meta-analyses (Moher et al., 2009).

2.1. Data Sources and Searches

PubMed, EMBASE, the Cochrane Library of Systematic Reviews, Web of Science, China National Knowledge Infrastructure, WanFang databases and SinoMed databases were searched by using different combinations of free text and database specific index terms related to the topics (Appendix 1.). The studies were not restricted by date, language, or publication status. The following combined search term was used: (Storage, store, cryopreservation), (complete blood count, CBC,

2352-3964/© 2017 The Authors. Published by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).





CrossMark

Hemogram) AND (Comprehensive Metabolic Pane, CMP, Chemistry Panel, chemistry Screen).

2.2. Study Selection

Titles, abstracts, and full-text articles were screened independently by 2 reviewers, with discrepancies discussed with the research group. We used the following inclusion criteria:

- 1) Published or unpublished clinical trials in English or Chinese with the full text available;
- 2) Analysis were performed at once (0 h.);
- Sample was anticoagulated whole blood without any pretreatment (residual leucocyte, PAS, Pathogen reduction, etc);
- 4) Sample was stored under -20 °C, 4 °C, or RT;
- 5) Participants were adults.

And criteria for excluding studies were:

- 1) No data in humans
- No original research (reviews, editorials, non-research letters, protocols)
- 3) Sample was stored in open container;
- 2.3. Data Extraction

Paired reviewers independently and in duplicate screened full texts for eligible articles, extracted data from each eligible study and assessed the quality of evidence using MINORS tool. Discrepancies were



PRISMA 2009 Flow Diagram

reconciled after discussion. For each eligible study, information on baseline population characteristics was retrieved, including location, cases, sex and age distribution, collection volume and storage condition. If information was present only in figures, we planned to contact authors.

2.4. Outcome Measures

When 4 or more studies assessed the same outcome, it will be included. The final included CBC outcomes were WBC, PLt, MPV, RBC, HGB, MCHC, RDW, HCT, MCV, MCH. CMP outcomes were GLU, K, Na, Cl, LDH, AST, ALT, TP, ALB, TBIL, DBIL, TC, TG, Cr, BUN, ALP.

2.5. Statistical Analysis

Meta-analyses were conducted with the software Revman 5.3 and Stata 14.0. Studies were pooled within outcome measures, and standardized mean difference (SMD) and 95% CIs were constructed using fixed- or random-effects meta-analysis. Random effects were presented given the heterogeneity among studies where I² statistic > 50% (Higgins et al., 2003). Sensitive analysis was also performed to evaluate the influences of individual studies on the final effect. The Begg rank correlation (Begg and Mazumdar, 1994) and Egger regression asymmetry test (Egger et al., 1997) were used to examine publication bias. If publication bias was confirmed, a trim-and-fill method developed by Duval and Tweedie was implemented to adjust for this bias. Then, we replicated the funnel plot with their "missing" counterparts around the adjusted summary estimate.



Fig. 1. Flow chart showing the meta-analysis studies selection. A total of 1980 studies were identified, and 1213 studies were excluded because of duplication. After reading the titles and abstracts, 608 studies were excluded. 159 possible full text studies were carefully reviewed (no data for 0 h. [n = 35]; animal studies [n = 24]; review and meta-analysis [n = 11]). Finally, 89 trials were included for quantitative analysis.

Table 1
Characteristics of eligible studies.

First author (year)	Cases	Male/Female	age	Sample collection	Sample storage	Parameter	MINOR
Ai, WJ 2015	82	46/36	27.8 ± 2.8	6	4 °C, RT, 35 °C	HCT, HGB, MCHC, PLt, RBC, RDW, WBC	22
Bian, S 2014	50	U	U	U	−20 °C, 4 °C, RT	ALB, ALT, AST, CK, Cl, GLU, K, LDH, Na	22
Cai, J 2017	200	111/89	38.32 ± 6.46	1.5	RT	GLU	22
Chen, C 2004	40	33/7	22-50	U	RT	PLt, RBC, WBC	22
Cui, LN 2016	50	25/25	30.8 ± 7.7	U	−20 °C, 4 °C, RT	ALB, ALT, AST, CK, CO2, GLU, K, LDH, Na, TP	22
Cui, QL 2012	5	U	U	U	4 °C, RT	ALB, ALT, AST, BUN, CK, DBIL, GLU, TBIL, TC, TG, TP, UA	22
Cui, RG 2013	150	87/63	19-40	4	RT	Ca, Cl, CO2CP, K, Na	22
Daves, M 2015	16	11/5	35-89	U	4 °C, RT, 35 °C	MCHC, MCV, MPV, PLt, RBC, RDW, WBC	22
Deng, ZK 2012	30	U	U	U	−20 °C, 4 °C, RT	ALB, ALT, AST, CK, Cl, CO2, GLU, K, LDH, Na, TP	22
Dong LM 2014	200	100/100	38.7 ± 6.5	5	RT	HGB, MCHC, MCV, PLt, RBC, WBC	22
Fan, YH 2015	88	56/32	37.2 ± 4.7	6	RT	ALT, BUN, Cl, Cr, DBIL, GLU, K, Na, TBIL	22
Gao, HE 2015	86	44/42	37.5 ± 3.2	2	RT	PLt, WBC	22
Gao, YH 2016	126	83/43	44.1412.93	8	- 20 °C, 4 °C, RT	ALB, ALT, AST, CK, Cl, GLU, K, LDH, Na	22
Ge, LF 2009	50	25/25	34.5	2	4 °C	HCT, MCV, MPV, PLt, RBC, WBC	22
Gong, OH 2013	91	29/62	28-50	2	4 °C. RT	HCT, HGB, MCHC, MCV, PLt, RBC, RDW, WBC	22
Guo, HX 2017	200	U	51.6 + 2.3	U	RT	ALT, AST, CK, CK-MB, α-HBDH, GLU, LDH	22
Han IP 2015	300	121/179	16-68	Ū	RT	HGB PLt RBC WBC	22
Hu HI 2013	10	121,170	II II	U U	BT	ALP ALT AST GGT IDH	22
Hu HV 2015	240	U	U	U U	BT	HCB PLt RBC W/BC	22
Huang CO 2012	240	U	U	2	A°C PT	HCD DI+ DDC WDC	22
Hunna CE 2013	160	80/80	312 + 42	2 5	PT	HCT HCR MCHC MCV DI+ DDC DDW WDC	22
Huang VP 2012	100	00/00	31.2 ± 4.3	Э 4	κι 4°C	HCT, HGD, WILTC, WILV, FLL, KBC, KDWV, WBC	22
Fudily, AK 2012	40	U 55/25		4	4 U 4°C	ICE DITERED WICH, WICH, WICY, WIPV, PLE, KBC, KDW, WBC	22
JId, DP 2010	90	35/35	50 ± 0.5	0	4 U	ILCE MELC MEL DIA DEC DEVI MEC	22
Jiang, RR 2013	30	U	U	4	4 °C, R1	HCI, HGB, MCHC, MCV, PLt, RBC, RDW, WBC	22
Jiao, YH 2016	86	47/39	29.58 ± 7.15	20	KI	ALI, ASI, BUN, DBIL, GLU, K, Na, TBIL	22
Jin, LY 2011	30	13/17	20-60	U	RT	HCT, HGB, MCH, MCHC, MCV, PLt, RBC, WBC	22
Kang, LX 2016	76		U	U	RT	AST, CK, CK-MB, α-HBDH, GLU	22
Li, M 2016	124	74/50	37.4 ± 8.2	2	RT	ALT, AST, BUN, Ca, GLU, P, TBIL, TP	22
Li, N 2015	40	20/20	14-62	2	4 °C	HCT, HGB, MCHC, MCV, PLt, RBC, RDW, WBC	22
Li, QZ 2011	60	35/25	32.3 ± 8.3	U	4 °C, RT	RBC, Hb, HCT, WBC, PLt, RDW	22
Li, Y 2012	40	U	U	8	−20 °C, 4 °C, RT, −80 °C	ALT	22
Li, YF 2015	160	94/66	35.11 ± 10.64	0.6	RT	HGB, PLt, RBC, WBC	22
Li, YJ 2015	1000	500/500	31.57 ± 3.24	U	-20 °C	ALT, UA, ALB, BUN, TP, CR, TBIL, TC, CK	22
Li. 7S 2014	76	31/45	43.2 ± 11.8	U	RT	PLt.WBC	22
Liang 0 2004	40	16/24	45.7	2	4 °C RT	HCT HGB MPV PIT RBC RDW WBC	22
Liu HS 2006	20	10,21	U	4	4 °C	HCT HGB MCH MCHC MCV MPV PIt RBC RDW WBC	22
Liu, NV 2008	60	U	U	2	4 °C	HCT HCB MCHC MCV PIt RBC RDW WBC	22
Liu, W 2015	136	75/61	395 ± 65	3	PT	WBC RBC DIt Hb	22
Liu, W 2015	60	20/22	12 71	л П	A°C	UCT UCP MCU MCUC MCV MDV DI+ PPC PDW	22
LUIIg, IIA 2000	20	20/32	13-71	2	4 C	HCT, HGD, MCH, MCHC, MCV, MFV, FL, KDC, KDVV	22
IVId, L 2013	30	18/12	22 ± 3	2	4 C, KI, 35 C	HUL, MUHU, KDW	22
Peng, HW 2010	15/	U	U	2	-20 C	ALB, ALI, ASI, BUN, CI, GLU, IBIL, IP, UA	22
Qian, M 2011	15	0	U	0		HCI, HGB, MCH, MCHC, MCV, MPV, PLT, KBC, KDVV, WBC	22
Qu, SJ 2014	80	49/31	39.57 ± 3.67	10	- 20 °C, R1,	BUN, CI, Cr, α-HBDH, GLU, K, Na, PLt, IBIL	22
Rui, F 2015	120	86/52	33.75 ± 7.67	U	RI	HGB, PLt, RBC, WBC	22
Shi, ZZ 2006	5	U	U	5	4 °C, RT	ALB, CI, GLU, K, Na, TC, TG, TP, UA	22
Sirdah, MM 2013	25	25/0	18-20	20	4 °C, RT	HCT, HGB, MCHC, MCV, PLt, RBC, RDW, WBC	22
Su, QJ 2007	47	26/21	29.6 ± 8.4	U	4 °C, RT	HCT, HGB, MPV, PLt, RBC, RDW, WBC	22
Su, YH 2011	33	U	U	U	RT	GLU	22
Sun, DJ 2015	160	89/71	46.3 ± 2.7	2	RT	HCT, HGB, MCH, MCHC, MCV, MPV, PLt, RBC, WBC	22
Tan, FS 2011	35	23/12	19-68	1	RT	HGB, PLt, RBC, WBC	22
Tian ML 2015	100	U	U	U	−20 °C, 4 °C, RT	ALB, ALP, AST, CK-MB, DBIL, LDH, TBIL	22
Wang, J 2016	200	100/100	39.0 ± 9.6	5	4 °C, RT	HGB, PLt, RBC, WBC	22
Wang, LL 2016	30	13/17	18-43	U	4 °C, RT	HCT, HGB, MCHC, MCV, PLt, RBC, RDW, WBC	22
Wang, OP 2006	50	28/22	16-60	U	4 °C	HCT, HGB, MCH, MCHC, MCV, MPV, PLt, RBC, RDW, WBC	22
Wang, WS 2016	80	45/35	24-54	2	RT	PLt. WBC	22
Wang Y 2009	40	33/7	22-50	- U	RT	PLt RBC WBC	22
Wang YC 2003	30	18/12	11 11	4	4°C RT	HCB PIT RBC WBC	22
Wallg, 10 2014	20	10/12	10 40	5	4°C	ALP ALP ALT AST PLIN C2 CL CCT CLU K N2 D TPU	22
vvalig, 1j 2011	00	40/40	13-40	J	чι	רבט, רובר, הבד, הסד, טטוז, כמ, כו, טטוז, GLU, K, INd, F, IBIL, דר דר דם	22
Ma: CE 2014	150	70/70			4.90	IC, IC, IF	22
vvel, Sr 2014	150	10/12		U	4 L	ALP, ALI, ASI, BUN, CA, GGI, GLU, P, IBIL	22
vvei, SJ 2016	/1	33/38	50.85 ± 5.85	2	4 C, KI	HGB, PLT, KBC, WBC	22
wen, XM 2008	10	U	U	5.5	4 °C, KI	HCI, HGB, MCH, MCHC, MCV, PLt, RBC, RDW, WBC	22
Wood, B L 1999	252	U	U	U	4 °C, RT	HCT, HGB, MCH, MCHC, MCV, PLt, RBC, WBC	22
Wu, HL 2011	33	15/18	18-68	3	4 °C	HCT, HGB, MCV, MPV, PLt, RBC, WBC	22
Wu, YY 2006	30	15/15	21-45	2	4 °C, RT	HCT, HGB, MCV, PLt, RBC, WBC	22
Xiao, XY 2013	70	45/25	23-26	2	4 °C, RT, 35 °C	HCT, MCHC, RDW	22
Xu, JF 2012	120	60/60	18-65	U	4 °C	ALB, ALP, ALT, AST, BUN, Ca, Cl, GGT, GLU, K, Na, P, TBIL, TC, TG, TP	22
	53	30/23	32.20 + 5.45	10	4 °C, RT	ALB, GLU, K, TP, UA,	22
Yan. F 2015		20/40	262 20	4	4 °C	ALB ALP ALT AST TBIL TG TP	22
Yan, F 2015 Yang XR 2013	80	32/48	$\gamma \gamma + \gamma \gamma$				in he
Yan, F 2015 Yang, XR 2013 Yang, YM 2015	80 120	32/48 U	50.5 ± 5.9	л П	4 °C	ALP ALT AST CK-MB CILLUDH	22
Yan, F 2015 Yang, XR 2013 Yang, YM 2015 Yang, 7M 2016	80 120 60	32/48 U U	50.5 ± 5.9 U	U U	4 °C — 20 °C	ALP, ALT, AST, CK-MB, GLU, LDH ALB, ALT, AST, CK-MB, CLU, TBU, TP, UA	22

(continued on next page)

Table 1 (continued)

First author (year)	Cases	Male/Female	age	Sample collection	Sample storage	Parameter	MINORS
Yi, JP 2014	68	37/31	43.7 ± 12.6	U	−20 °C	ALB, ALT, AST, BUN, Cr, GLU, TBIL, TP, UA	22
Yu, DQ 2015	86	47/39	29.58 ± 7.15	20	RT	ALT, AST, BUN, DBIL, GLU, K, Na, TBIL	22
Yu, FR 2015	172	94/78	U	20	RT	ALT, AST, BUN, DBIL, GLU, K, Na, TBIL	22
Yu, SQ 2003	60	34/26	19-65	0.5	RT	HGB, PLt, RBC, WBC	22
Zeng, ZL 2007	30	U	U	5	4 °C, RT	ALB, ALP, ALT, AST, CK, Cr, DBIL, GLU, TBIL, TC, TG, TP, UA	22
Zhang, JS 2015	200	60/40	46.0 ± 2.0	U	RT	ALT, AST, CK, CK-MB, C, Cr, α-HBDH, GLU, K, LDH, Na,	22
						TBIL, UA	
Zhang, TY 2014	10	U	U	3	4 °C, RT	ALB, ALT, AST, BUN, CK, Cl, Cr, DBIL, α -HBDH, GLU, K, Na,	22
						TBIL, TC, TG, TP, UA	
Zhang, YM 2014	86	U	U	2	RT	ALT, AST, DBIL, TBIL	22
Zhang, ZQ 2005	10	U	U	15	RT	Cl, CO2CP, GLU, K, Na	22
Zheng, G 2013	50	U	U	U	-20 °C	ALB, ALT, AST, BUN, Cr, GLU, TBIL, TP, UA	22
Zheng, HF 2016	120	60/60	29.6 ± 3.7	U	4 °C, RT	ALB, ALT, AST, BUN, CK, GLU, TBIL, TC, TG, TP	22
Zhou, YJ 2013	40	U	U	U	4 °C, RT	HGB, PLt, RBC, WBC	22
Zhou, YX 2006	50	18/32	14-70	U	4 °C	HCT, HGB, MCH, MCHC, MCV, MPV, PLt, RBC, RDW	22
Zhu, JH 2014	120	64/56	30.3 ± 2.1	U	4 °C, RT	ALB, ALT, AST, BUN, CK, GLU, TC, TP	22
Zhu, Q 2012	100	61/39	19.5 ± 8.5	8	4 °C, RT	GLU	22
Zhu, TL 2014	330	U	40.27 ± 11.06	3	RT	ALT, AST, γ-GGT, TBIL	22
Zhu, WY 2011	86	40/46	4-82	2.5	RT	HCT, HGB, MCH, MCHC, MCV, MPV, PLt, RBC, RDW, WBC	22
Zou, HY 2016	70	37/33	21-61	2	RT	HGB, PLt, RBC, WBC	22

Note: HCT: hematocrit; HGB: hemoglobin; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; MCV: mean corpuscular volume; MPV: mean platelet volume; PLt: platelet count; RBC: red blood cell count; RDW: RBC distribution width; WBC: white blood cell count; ALB: albumin; ALP: alkaline phosphatase; ALT: alanine amino transferase; AST: aspartate amino transferase; BUN: blood urea nitrogen; Ca: Calcium; CK: creatine kinase; CK-MB: creatine kinase isoenzymes; Cl: Chloride; CO₂: carbon dioxide; Cr: creatinine; DBLL: direct bilirubin; α -HBDH: α - hydroxybutyrate; GGT: γ – -glutamyl transferase; GLU: glucose; K: potassium; LDH: lactate dehydrogenase; Na: sodium; P: phosphorus; TBLL: total bilirubin; TC: total cholesterol; TG: triglyceride; TP: total protein; UA: uric acid; MINORS: Methodological index for non-randomized studies.

3. Results

3.1. Literature Search

A total of 1980 studies were identified, and 1213 studies were excluded because of duplication. After reading the titles and abstracts, 608 studies were excluded. 159 possible full text studies were carefully reviewed (no data for 0 h. [n = 35]; animal studies [n = 24]; review and meta-analysis [n = 11]). Finally, 89 trials were included for quantitative analysis (Fig. 1). Their characteristics are summarized in Table 1.

3.2. CBC

3.2.1. WBC Count

33 studies (17,407 samples, Fig. S1) under RT and 22 studies (10,982 samples, Fig. 2) under 4 °C were enrolled. WBC count was relatively stable and the results had no significant change up to 3 d regardless of the storage temperature. For 5 d, differences were seen at 4 °C but had no data at RT.

3.2.2. Platelet Related Measurements

35 studies (18,012 samples, Fig. S2) at RT and 19 studies (7549 samples, Fig. 3) under 4 °C measured PLt count. At RT, even though tested 2 d later, there were no differences. Interestingly, at some time-points (1, 2 and 4 h.), PLt count was a little lower. Storage at 4 °C showed much more stability. Except 8 h., there were no statistical changes up to 3 d. MPV was not a very stable measurement for samples stored over time. It changed at the first compared time (1 h.) and no had differences for storage temperature (Fig. S3).

3.2.3. RBC Related Measurements

We included 31 studies (19,310 samples, Fig. 4) under RT and 22 studies (10,142 samples, Fig. S4) under 4 °C in the RBC count meta-analysis. The sample was stable for 24 h. at RT. However, even just 12 h. later, the results had changed at 4 °C. For MCHC, the specimens stored at 4 °C were stable <12 h., but if at RT, 24 h. showed no difference (Fig. S5). HGB comparison of 1 h., 2 h. and 4 h. were statistically significant, but exhibited no difference over time (up to 3 d) under RT. Samples were significantly different from 2 d onwards at 4 °C (Fig. S6). There was no statistically significant until 12 h. under RT for RDW which

decreased dramatically from 24 h., but was limited when stored at (4 °C) (Fig. S7). HCT was also a parameter that changed approximately at 8 h. at RT and were greatly dependent on storage temperature. Even though the sample had been stored for 5 d under 4 °C, it still exhibited no significant difference (Fig. S8). 8 h. after collection, MCV changed significantly in samples at RT. And 4 °C samples were significantly different only at 24 h. but not for 2 d or more (Fig. S9). During 3 d, we did not observe any differences for MCH (Fig. S10).

3.3. CMP

3.3.1. GLU

22 studies (9814 samples, Fig. S11) under RT, 11 studies (2638 samples, Fig. 5) under 4 °C and 8 studies (1852 samples, Fig. S12) under -20 °C measured GLU. Even the sample was stored for only 1 h at RT, the stability was unsatisfactory. Storage at 4 °C was much better and was stable up to 24 h. At 7 d storage there was stability but not for 14 d at -20 °C.

3.3.2. Electrolyte

The sample potassium was not very stable under RT and 1 h. storage had differences (Fig. S13). The results of Na changed at 12 h. under RT, and remained unchanged up to 24 h. under 4 °C (Fig. S14). For Cl, two-day under 4 °C were stable while 24 h. under RT had a difference (Fig. S15).

3.3.3. Enzyme and Protein

For 12 h., samples LDH under RT were statistically different, but the results were much better if stored under 4 °C (Fig. S16). Samples for AST had no difference for 24 h. for both RT and 4 °C. Storage for 7 d under -20 °C demonstrated statistical differences (Fig. S17), so was ALT (Fig. S18). ALP was stable for 24 h. under both RT and 4 °C (Fig. S19). TP was no difference up to 24 h. under RT but the results had changed for 12 h. under 4 °C (Fig. S20). ALB had stable results up to 24 h. under RT or 4 °C and could be stored for at least for 7 d under -20 °C(Fig. S21).

3.3.4. Other Parameters

Samples stored at 4 $^{\circ}$ C were stable up to 12 h., while 3 h. under RT showed differences for TBIL (Fig. S22). DBIL were stable both for 24 h. at RT and 4 $^{\circ}$ C(Fig. S23), so as TC (Fig. S24)and TG (Fig. S25). Sample

Study or Subgroup	Control Experimental Mean SD Total Mean SD T	nl Std. Mean Difference Fotal Weight IV, Random, 95% Cl	Std. Mean Difference IV. Random, 95% Cl
1.2.1 1hr Ai, WJ 2015 Jiang, RR 2013 Li, Q2 2011 Wang, YG 2014 Subtotal (95% Cl) Heterogeneity: Tau ² = 0.00;	5.82 1.35 82 5.79 1.32 6.18 1.73 30 6.33 1.79 5.9 0.7 30 6.1 0.7 5.43 1.16 30 5.46 1.19 172 Chi ^P =1.04, df=3 (P=0.79); I ^P =0%	82 1.5% 0.02 [-0.28, 0.33] 30 0.5% -0.08 [-0.59, 0.42] 30 0.5% -0.28 [-0.79, 0.23] 30 0.5% -0.03 [-0.53, 0.48] 172 3.1% -0.06 [-0.27, 0.15]	
Testfor overall effect: Z = 0. 1.2.2 hr Al, WJ 2015 Ge, LF 2009 Jia, DP 2016 Lianoz 0.2004 Liu, GY 2008 Wang, VG 2014 Wang, VG 2014 Wang, VG 2014 Wang, VG 2014 Heterogeneity: Tsu [#] = 0.00; Test for overall effect: Z = 0.00;	53 (P = 0.60) 5.82 1.36 82 5.76 1.31 6 0.39 50 6 0.38 6.32 0.89 90 6.33 0.85 7.56 2.72 40 7.65 2.72 6.33 0.36 60 6.38 0.36 5.35 1.64 200 6.21 1.72 5.43 1.16 30 6.24 1.14 6.78 1.98 612 6.83 1.8 Chil* = 1.71, df = 8 (P = 0.99); l* = 0% 12 (P = 0.91)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
1.2.4 4 hr AI, WJ 2015 Huang, CR 2013 Huang, CR 2012 Jiang, RR 2013 Li, QZ 2011 Lia, HS 2006 Liu, HS 2006 Liu, QY 2008 Su, QJ 2007 Wang, L 2016 Wang, L 2016 Wang, U 2016 Wang, CL 2016 Heterogeneity: Tau [*] = 0.00; Test for overall effect. Z = 1.1	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
1.2.5.6 µr A, WJ 2015 Ja, DP 2016 Liang, Q 2004 Wang, LL 2016 Wang, YJ 2014 Wang, YJ 2014 Subtotal (95% C) Heterogeneity: Tau ^e = 0.00; Test for overall effect Z = 0.	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	82 1.5% 0.09 [-0.22, 0.40] 16 0.3% 0.03 [-0.67, 0.72] 90 1.6% 0.01 [-0.28, 0.30] 40 0.7% 0.00 [-0.44, 0.44] 30 0.5% 0.06 [-0.44, 0.57] 30 0.5% -0.01 [-0.51, 0.56] 318 5.8% 0.04 [-0.12, 0.19]	
1.2.6 8 hr Ai, WJ 2015 Ge, LF 2009 Jiang, RR 2012 Jiang, RR 2013 Li, OZ 2011 Li, OZ 2001 Su, GJ 2007 Wang, J 2016 Wang, J 2016 Wang, VG 2014 Wang, VG 2014 Wang, VG 2014 Test for overall effect. Z = 3.00; Test for overall effect. Z = 3.00;	$ \begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
1.2.7 12 lur Al, WJ 2015 Luu, GJ 2013 Luu, GJ 2008 Su, GJ 2007 Wang, YG 2014 Wu, YY 2008 Subtotal (95% Cl) Heterogeneity: Tau [#] = 0.00; Test for overall effect Z = 0.	5.82 1.35 82 5.83 1.25 7.64 1.2 200 7.86 1.1 6.33 0.36 60 6.27 0.36 6.7 0.7 30 6.6 0.6 5.43 1.16 30 5.48 1.18 6.76 1.98 30 6.69 1.92 Chi ^a = 1.50, df = 5 (P = 0.91); ^a = 0% 78 (P = 0.43)	82 1.5% 0.15 [-0.16, 0.45] 200 3.7% -0.02 [-0.21, 0.16] 60 1.1% 0.17 [-0.16, 0.52] 30 0.5% 0.15 [-0.36, 0.66] 30 0.5% 0.05 [-0.46, 0.52] 30 0.5% 0.05 [-0.46, 0.55] 30 0.5% 0.05 [-0.46, 0.55] 432 7.9% 0.05 [-0.08, 0.19]	
1.2.8.24 hr Ai, WJ 2015 Daves, M 2015 Ge, LF 2009 Gong, GH 2013 Gong, GH 2013 Jiang, RR 2013 Li, GZ 2011 Liu, GY 2008 Liu, GY 2008 Gu, GJ 2007 Wang, LL 2016 Wang, VG 2014 Wood, BL (health) 1999 Wood, BL (health) 1999 Wood, SL (00111) 1999 Subtotal (95% CL) Heterogeneity: Tau [*] = 0.00; Test for overall effect Z = 1.	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
1.2.9.2.4 Ai, WJ 2015 Gong, GH 2013 Huang, GG 2013 Li, GZ 2011 Su, G, HX007 Wang, LC 2016 Wang, GP 2005 Wang, YG 2014 Zhou, YX 2008 Heterogeneity: Tau [*] = 0.00; Test for overall effect. Z = 1.	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
1.2.10 3 d Ai, WJ 2015 Gong, GH 2013 Huang, CG 2013 Long, HX 2006 Su, GJ 2007 Wang, LL 2016 Wang, GP 2006 Wang, GP 2006 Wang, YG 2014 Zhou, YX 2006 Subtotal (95% CI) Heterogeneity, Tau ² = 0.00; Test for overall effect Z = 1.	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
1.2.114 d L, GZ 2011 Long, HX 2006 Su, GJ 2006 Zhou, YX 2008 Subtotal (95%-CI) Heterogeneiky: Tau [#] = 0.03; Test for overall effect: Z = 1.1		30 0.5% 0.49 [-0.02, 1.00] 60 1.1% 0.08 [-0.28, 0.44] 30 0.5% 0.89 [0.16, 1.21] 50 0.9% 0.01 [-0.38, 0.40] 50 0.9% 0.08 [-0.31, 0.47] 220 4.0% 0.22 [-0.02, 0.46]	
1.2.12 5 d L, $_{0Z}$ 2011 Long, HX 2006 Su, $_{QJ}$ 2007 Wang, $_{QP}$ 2008 Zhou, YX 2008 Subtotal (95% Cl) Heterogeneily: Tau ² = 0.05; Test for overall effect: Z = 2.	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	30 0.5% 0.66 [0.14, 1.18] 60 1.1% 0.16 [-0.20, 0.52] 30 0.5% 0.80 [0.27, 1.33] 50 0.9% 0.01 [-0.38, 0.41] 50 0.9% 0.16 [-0.23, 0.55] 220 3.9% 0.31 [0.04, 0.59]	
Total (95% Cl) Heterogeneity: Tau ² = 0.00; Test for overall effect: Z = 4.; Test for subgroup difference	5491 5 Chi ² = 67.30, df = 97 (P = 0.99); i ² = 0% 22 (P < 0.0001) es: Chi ² = 13.25, df = 10 (P = 0.21), i ² = 2	5491 100.0% 0.08 [0.04, 0.12] - 24.5%	-1 -0.5 0 0.5 1 Favours [Control] Favours [Experimental]

Fig. 2. Forest plot of store effect on WBC count under 4 °C. 22 studies (10,982 samples) under 4 °C were enrolled. WBC count was relatively stable and the results had no significant change up to 3 d. For 5 d, differences were seen.

2.2.2 2 hr 3e, LF 2009 IIa, DP 2016	Mean	ntrol SD	Total	Expe Mean	rimental SD	Total	Weight	Std. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl
lia, DP 2016	24.5.0	50.0	~~	24.1.2	510	~	4.5%	0.001.0.00.0.40	
14, 01 2010	215.8	24.25	50	214.2	54.2 20.44	90	1.5%	1.08.0.76.1.39	
.i, QZ 2011	192	11	30	183	11	30	1.6%	0.81 [0.28, 1.34]	
Liang, Q 2004	225.8	82.2	40	220.4	80.5	40	1.5%	0.07 [-0.37, 0.50]	
Vang, J 2016	218	32	200	223	34	200	1.6%	-0.15 [-0.35, 0.05]	
90, YY 2006 Subtotal (95% CD	225.1	50.5	30	224.22	54.22	30	1.5%	0.02 [-0.49, 0.52]	•
Heterogeneity: Tau ² = 0.29; C	:hi² = 49.17,	, df = 5 (F	P < 0.0	0001); l²:	= 90%	440	5.0 %	0.50 [-0.10, 0.77]	
Test for overall effect: Z = 1.25	3 (P = 0.20)								
2.4 4 hr Huang, CQ 2013	194.58	11.58	200	194.08	10.5	200	1.6%	0.05 (-0.15, 0.24)	+
luang, XR 2012	228	11.3	40	228	11.3	40	1.5%	0.00 [-0.44, 0.44]	
iang, RR 2013	196.46	50.6	30	178.1	58.9	30	1.5%	0.33 [-0.18, 0.84]	
i, QZ 2011	192	11	30	182	10	30	1.4%	0.94 [0.40, 1.47]	
Jang, Q 2004	225.8	82.2	40	217.9	80.4	40	1.5%	0.10 [-0.34, 0.53]	
u, QJ 2007	191	11	30	194	10	30	1.5%	-0.28 [-0.79, 0.23]	
(ang, J 2016	218	32	200	239	36	200	1.6%	-0.62 [-0.82, -0.41]	
/ang, LL 2016	199.7	24	30	198.4	24	30	1.5%	0.05 [-0.45, 0.56]	
(u, YY 2006 ubtotal (95% CI)	225.1	50.5	30 650	215.3	51.64	30 650	1.5%	0.19 [-0.32, 0.70] 0.05 [-0.23, 0.33]	•
leterogeneity: Tau ² = 0.15; C est for overall effect: 7 = 0.3;	$hi^2 = 47.80$, 5 (P = 0.73)	, df = 9 (f	P < 0.0	0001); I*:	= 81%			•	
256 br	, - 0.1 of								
aves, M 2015	262 1	194.87	16	252.31	195.28	16	1.4%	0.05 [-0.64, 0.74]	
jang, Q 2004	225.8	82.2	40	217.8	80.2	40	1.5%	0.10 [-0.34, 0.54]	_ +
vang, J2016 Vang II 2016	218	32	200	254	35	200	1.6%	-1.07 [-1.28, -0.86]	
Vu, YY 2006	225.1	50.5	30	215.44	54.6	30	1.5%	0.18 [-0.33, 0.69]	<u>+</u>
ubtotal (95% CI)			316	2.2.44	-4.0	316	7.3%	-0.14 [-0.82, 0.53]	+
eterogeneity: Tau ² = 0.53; C est for overall effect: Z = 0.41	hi ^a = 49.87, 1 (P = 0.68)	df=4 (1	P < 0.0	0001); I*:	= 92%				
.2.6 8 hr	,								
e, LF 2009	215.8	50.3	50	205.4	54	50	1.5%	0.20 [-0.20, 0.59]	+
iang, AR 2012	196.46	11.3	40	211	48.8	40	1.5%	1.52 [1.02, 2.02]	
i, QZ 2011	192	11	30	180	11	30	1.4%	1.08 [0.53, 1.62]	
iu, HS 2006	228	11.3	20	211	10.9	20	1.4%	1.50 [0.79, 2.21]	
u, QJ 2007	191	11	30	192	11	30	1.5%	-0.09 [-0.60, 0.42]	_
/ang, LL 2016	199.7	24	30	195.9	22	30	1.5%	0.16 [-0.34, 0.67]	
ubtotal (95% CI)	225.1	00.0	260	201.1	49.9	260	11.6%	0.60 [0.18, 1.03]	•
leterogeneity: Tau ² = 0.30; C est for overall effect: 7 = 2.70	hi ² = 38.55, 9 (P = 0.004	, df = 7 (f	P < 0.0	0001); I*:	= 82%				
2.8 24 hr		·							
e, LF 2009	215.8	50.3	50	183.5	45.3	50	1.5%	0.67 [0.27, 1.07]	
ong, QH 2013	229.58	78.8	31	230.16	78.63	31	1.5%	-0.01 [-0.51, 0.49]	_ +
luang, CQ 2013	194.58	11.58	200	210.54	10.22	200	1.5%	-1.46 [-1.68, -1.24]	
iuang, XR 2012 iang, RR 2013	196.46	11.3 50.6	40	234	52.9	40	1.5%	-0.51 [-0.96, -0.06] 0.14 L0 37 0.641	
i, QZ 2011	192	11	30	163	11	30	1.4%	2.60 [1.90, 3.30]	
iu, HS 2006	228	11.3	20	234	12	20	1.4%	-0.50 [-1.14, 0.13]	
ong, HX 2006	210	70	60	204	71.3	60	1.5%	0.08 [-0.27, 0.44]	±
u, QJ 2007	191	11	30	187	11	30	1.5%	0.36 [-0.15, 0.87]	
(and BI (health) 1999	265	46	20	190.5	24.8	20	1.5%	0.13 [-0.38, 0.64]	
Vood, BL (patient) 1999	246	87	98	249	87	98	1.5%	-0.03 [-0.31, 0.25]	-
hou, YX 2006	210	70	50	204	71.3	50	1.5%	0.08 [-0.31, 0.48]	+
subtotal (95% Cl) Heterogeneity: Tau² = 0.76; C	hi² = 220.34	6, df = 1:	689 2 (P < (0.00001);	I² = 95%	689	19.1%	0.09 [-0.40, 0.58]	-
est for overall effect: Z = 0.36	3 (P = 0.72)								
.2.9 48 hr	229 58	78.8	31	235 42	79.55	31	1.6%	-0.07 E0.57 0.431	
luana, CQ 2013	194.58	11.58	200	218.69	10.87	200	1.5%	-2.14 (-2.39, -1.90)	
i, QZ 2011	192	11	30	160	12	30	1.4%	2.74 [2.03, 3.46]	
ong, HX 2006	210	70	60	197	70	60	1.5%	0.18 [-0.17, 0.54]	+-
u, QJ 2007 (ang. LL 2016	191	11	30	185	12	30	1.5%	0.51 [-0.00, 1.03]	
ang, LL 2016 (ang, QP 2006	206 7	70 1	30	205.2	25.6	50	1.5%	0.20 [-0.30, 0.71] 0.02 [-0.37 0.41]	<u> </u>
hou, YX 2006	210	70	50	197	70	50	1.5%	0.18 [-0.21, 0.58]	<u>+</u>
ubtotal (95% CI)			481			481	11.8%	0.19 [-0.78, 1.15]	-
eterogeneity: Tau ² = 1.87; C	hi² = 306.99 8 (P = 0.71)	9, df = 7	(P < 0.	00001); F	°= 98%				
est for overall effect: Z = 0.38									
est for overall effect: Z = 0.34 2.10 72 hr				010 55	00	31	4 500		
est for overall effect: Z = 0.34 2.10 72 hr long, QH 2013	229.58	78.8	31	240.55	82		1.5%	-0.13 [-0.83, 0.36]	
est for overall effect: Z = 0.34 2.10 72 hr long, GH 2013 luang, CQ 2013 . 07 2014	229.58 194.58	78.8 11.58	31 200	225.68	10.84	200	1.5%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49]	
esu for overall effect: Z = 0.34 .2.10 72 hr long, QH 2013 luang, CQ 2013 l, QZ 2011 one, HV 2006	229.58 194.58 192 210	78.8 11.58 11 70	31 200 30 60	240.55 225.68 155 202	10.84 13 74 2	200 30	1.5% 1.5% 1.3%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49] 3.03 [2.28, 3.79] 0.11 [-0.25 0.47]	
est for overall effect: Z = 0.34 2.10 72 hr long, GH 2013 lueng, CQ 2013 l, QZ 2011 ong, HX 2006 u, GJ 2007	229.58 194.58 192 210 191	78.8 11.58 11 70 11	31 200 30 60 30	240.55 225.68 155 202 180	10.84 13 74.2 13	200 30 60 30	1.5% 1.5% 1.3% 1.5% 1.5%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49] 3.03 [2.28, 3.79] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43]	- +
est for overall effect: Z = 0.34 2.10 72 hr ong, GH 2013 ueng, CQ 2013 i, GZ 2011 ong, FK 2006 u, GJ 2007 (ang, LL 2016	229.58 194.58 192 210 191 199.7	78.8 11.58 11 70 11 24	31 200 30 60 30 30	240.55 225.68 155 202 180 190.4	82 10.84 13 74.2 13 25.8	200 30 60 30 30	1.5% 1.3% 1.5% 1.5% 1.5%	-0.13 [+0.83, 0.36] -2.77 [+3.04, -2.49] 3.03 [2.28, 3.79] 0.11 [+0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [+0.14, 0.88]	- +
est tor overall effect: Z = 0.31 2.10 72 hr ong, GA 2013 uang, CG 2013 i, GZ 2011 ong, HX 2006 u, GJ 2007 iang, LL 2016 iang, CD 2006 u, W 2006	229.58 194.58 192 210 191 199.7 206.7	78.8 11.58 11 70 11 24 70.1	31 200 30 60 30 30 50	240.55 225.68 155 202 180 190.4 205.3	82 10.84 13 74.2 13 25.8 71.2	200 30 60 30 30 50	1.5% 1.3% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49] 3.03 [2.28, 3.79] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.02 [-0.37, 0.41]	- +
est tor overall effect: Z = 0.31 2.10 72 hr ioong, GH 2013 lueng, CQ 2013 l, GZ 2011 ong, HX 2005 u, GJ 2007 fang, LL 2018 fang, QP 2006 hou, YX 2006 lutotat (95% C)	229.58 194.58 192 210 191 199.7 206.7 210	78.8 11.58 11 70 11 24 70.1 70	31 200 30 60 30 30 50 50 481	240.55 225.68 155 202 180 190.4 205.3 202	82 10.84 13 74.2 13 25.8 71.2 74.2	200 30 60 30 30 50 50 481	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.83, 0.36] -2.77 [-3.04, -2.49] 3.03 [2.28, 3.78] 0.11 [-0.25, 0.47] 0.30 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.02 [-0.37, 0.41] 0.11 [-0.28, 0.50] 0.19 [-0.26, 1.33]	
est tor overall effect: Z = 0.31 2.10 72 hr ong, GH 2013 uang, CG 2013 i, GZ 2011 ong, HX 2005 u, GJ 2007 fang, LL 2016 fang, QP 2006 hou, YX 2006 lithotal (95% CI) eterogeneity: Tau ² = 2.68; C sel for overall effect Z = 0.38; C	229.58 194.58 192 210 191 199.7 206.7 210 hi ^p = 411.93 2 (P = 0.75)	78.8 11.58 11 70 11 24 70.1 70 7, df = 7	31 200 30 60 30 30 50 50 481 (P < 0.	240.55 225.68 155 202 180 190.4 205.3 202 00001); F	82 10.84 13 74.2 13 25.8 71.2 74.2 74.2	200 30 60 30 30 50 50 481	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.83, 0.36] -2.77 [-3.04, -2.49] 3.33 [2.28, 3.79] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.02 [-0.37, 0.41] 0.11 [-0.28, 0.50] 0.19 [-0.96, 1.33]	
ess tor overall effect: Z = 0.31 2.10 72 hr ong, CH 2013 uang, CG 2013 u, GZ 2011 ong, FK 2006 u, GJ 2007 fang, LL 2016 fang, CH 2016 latotal (95% Cf) elerogenehy. Tau ^a = 2.88; C elerogenehy. Tau ^a = 2.88; C	229.58 194.58 192 210 191 199.7 206.7 210 chi ² = 411.92 2 (P = 0.75)	78.8 11.58 11 70 11 24 70.1 70 7, df = 7	31 200 30 60 30 50 50 481 (P < 0.	240.55 225.68 155 202 180 190.4 205.3 202 000001); F	82 10.84 13 74.2 13 25.8 71.2 74.2 74.2 ?= 98%	200 30 60 30 30 50 50 481	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49] 3.03 [-28, 3.79] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.02 [-0.37, 0.41] 0.11 [-0.28, 0.50] 0.19 [-0.96, 1.33]	
est tor overall effect: Z = 0.31 2.10 72 hr ong, GH 2013 turang, CQ 2013 turang, CQ 2013 turang, CQ 2013 turang, CQ 2013 ong, LH 2006 turctoral (95 Ct) telerogeneity, Tau ² = 2.68; C est for overall effect: Z = 0.32 2.114 d 1, QZ 2011 turang, CQ 2	229.58 194.58 192 210 191 199.7 206.7 210 chi ^a = 411.97 2 (P = 0.75)	78.8 11.58 11 70 11 24 70.1 70 7, df = 7	31 200 30 60 30 50 50 481 (P < 0.	240.55 225.68 155 202 180 190.4 205.3 202 202 202 202 202 202 202	82 10.84 13 74.2 25.8 71.2 74.2 ?= 98%	200 30 60 30 30 50 50 481	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.83, 0.36] -2.77 [-3.04, -2.49] 3.03 [2.48] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.12 [-0.37, 0.41] 0.11 [-0.28, 0.50] 0.19 [-0.96, 1.33] 3.80 [2.76, 4.44]	
ess tor overall effect: Z = 0.31 2.10 72 hr ong, CH 2013 ueng, Co 2013 ong, CH 2013 ueng, L 2018 ang, LL 2018 ang, LL 2018 ang, LL 2018 ang, L2 2008 ang, L2 2018 ang, L2 201	229.58 194.58 192 210 191 199.7 206.7 210 :hi ² = 411.9i 2 (P = 0.75) 192 210	78.8 11.58 11 70 11 24 70.1 70 7, df = 7 11 70	31 200 30 60 30 50 50 481 (P < 0. 30 60 20	240.55 225.68 155 202 180 190.4 205.3 202 2020 200001); F	82 10.84 13 74.2 13 25.8 71.2 74.2 *= 98%	200 30 60 30 50 50 481 30 50 481	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49] 3.03 [-26, 3.78] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.26 [-0.37, 0.41] 0.11 [-0.26, 0.50] 0.19 [-0.96, 1.33] 3.60 [2.76, 4.44] 0.24 [-0.12, 0.60] 1.20 [0.66] -22	
ess tor overall effect: Z = 0.31 2.10 72 hr ong, GH 2013 ueng, CO 2013 1, 02 2011 ueng, LC 2006 ung, LK 2006 ung, LL 2016 fang, LP 2006 ubtotal (95% C) elerogenenity Tau* = 2.88; C elerogenenity Tau* = 2.88; C elerogenenity Tau* = 2.88; C elerogenenity Tau* = 2.88; C elerogenenity Tau* = 2.88; C ubtotal (95% C) elerogenenity Tau* = 2.88; C ubtotal (95% C) elerogenenity Tau* = 2.88; C ubtotal (95% C) elerogenenity Tau* = 2.88; C elerogenenity Tau* = 2.88; C eler	229.58 194.58 192 210 191 199.7 206.7 210 :hi ² = 411.9i 2 (P = 0.75) 192 210 192 210 192 210	78.8 11.58 11 70 11 24 70.1 70 7, df = 7 11 70 11 70.1	31 200 30 50 50 481 (P < 0. 30 60 30 50	240.55 225.68 155 202 180 190.4 205.3 202 20200001); F 150 193 177 205	82 10.84 13 74.2 13 25.8 71.2 74.2 *= 98% 12 72.9 12 70.8	200 30 60 30 50 50 481 30 60 30 50	1.5% 1.3% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.8%	$\begin{array}{c} -0.13 \left[+0.63, 0.36\right] \\ -2.77 \left[+3.04, -2.49\right] \\ 3.03 \left[+2.80, 3.79\right] \\ 0.11 \left[+0.25, 0.47\right] \\ 0.90 \left[+3.77, 1.43\right] \\ 0.37 \left[+0.14, 0.88\right] \\ 0.02 \left[+0.37, 0.41\right] \\ 0.11 \left[+0.28, 0.50\right] \\ 0.19 \left[+0.96, 1.33\right] \\ \end{array}$	
est tor overall effect: Z = 0.31 2.10 72 hr ong, GH 2013 tuang, CQ 2013 1, QZ 2011 ong, HX 2006 u, QJ 2007 Yang, LL 2018 Yang, LL 2018 Yang, LL 2018 Yang, LL 2018 Yang, LL 2018 Yang, LL 2018 Yang, LL 2018 efferogeneity. Tau ² = 2.88; C est for overall effect. Z = 0.32 2.11 4 d 1, QZ 2011 ong, HX 2006 u, QJ 2007 Yang, QP 2006 hou, VX 2006 LL 2006 JA 2007 YA 2006 JA 2006 JA 2007 YA 2006 JA 2006 JA 2007 YA 2006 JA 2007 YA 2006 JA 2007 YA 2006 JA 2007 JA 2007 JA 2006 JA 2007 JA 2007 JA 2007 JA 2007 JA 2006 JA 2007 JA 2006 JA 2007 JA 2006 JA 2007 JA 2006 JA 2007 JA 2006 JA 2007 JA 2006 JA 2006 JA 2007 JA 2006 JA 2006 JA 2007 JA 2006 JA 2006 JA 2006 JA 2006 JA 2007 JA 2006 JA 2006	229.58 194.58 192 210 191 199.7 206.7 210 :hi ² = 411.9i 2 (P = 0.75) 192 210 191 206.7 210	78.8 11.58 11 70 11 24 70.1 70 7, df = 7 11 70,1 70,1 70,1 70,1 70,1 70,1	31 200 30 60 30 50 50 481 (P < 0. 30 60 30 50 50 50	240.55 225.68 155 202 180 190.4 205.3 202 000001); F 150 193 177 205 193	82 10.84 13 74.2 13 25.8 71.2 74.2 *= 98% *= 98% 12 72.9 12 70.8 72.9	200 30 60 30 50 50 481 30 60 30 50 50	1.5% 1.3% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.8% 1.4% 1.5% 1.5%	$\begin{array}{c} -0.13 \left[+0.83, 0.36 \right] \\ -2.77 \left[+3.04, -2.49 \right] \\ 3.03 \left[+2.68, 3.78 \right] \\ 0.11 \left[+0.25, 0.47 \right] \\ 0.9 \left[+3.77, 1.43 \right] \\ 0.37 \left[+0.14, 0.88 \right] \\ 0.22 \left[+0.37, 0.41 \right] \\ 0.11 \left[+0.28, 0.50 \right] \\ 0.19 \left[+0.96, 1.33 \right] \\ \end{array}$	
est tor overail effect: Z = 0.31 .2.10 72 hr song, GH 2013 luteng, CQ 2013 J, QZ 2011 ang, HX 2006 w, QJ 2007 Yang, LL 2016 Yang, UZ 2016 whototal (95% C) leterogeneity. Tau ² = 2.88; C est for overail effect. Z = 0.32 .2.114 d J, QZ 2011 ang, HX 2006 w, QJ 2007 Yang, QP 2005 hou, YX 2006 uhitotal (95% C)) leterogeneity, Tau ² = 0.87; C	229.58 194.58 192 210 191 199.7 206.7 210 2(P = 0.75) 192 210 2(P = 0.75) 192 210 191 206.7 210 191 206.7 210	78.8 11.58 11 20 11 24 70.1 70 7, df = 7 11 70 11 70, 11 70, 1 70 11 70, 1 70 11	31 200 30 60 30 50 50 481 (P < 0. 30 50 50 50 50 220 P < 0.0	240.55 225.68 155 202 180 190.4 205.3 202 000001); F 150 193 177 205 193 00001); F	10.84 10.84 13 74.2 13 25.8 71.2 74.2 74.2 *= 98% 12 72.9 12 70.8 72.9 12 70.8 72.9	200 30 60 30 50 50 481 30 60 30 50 50 50 220	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	$\begin{array}{c} -0.13 \left[+0.83, 0.36 \right] \\ -2.77 \left[+3.04, -2.49 \right] \\ 3.03 \left[+2.68 \right] \\ 3.03 \left[+2.68 \right] \\ 0.11 \left[+0.25, 0.47 \right] \\ 0.21 \left[+0.37, 1.43 \right] \\ 0.37 \left[+0.14, 0.88 \right] \\ 0.22 \left[+0.37, 0.41 \right] \\ 0.11 \left[+0.26, 0.50 \right] \\ 0.19 \left[+0.96, 1.33 \right] \\ \end{array}$	
est for overall effect: $Z = 0.31$.2.10 72 hr song, GH 2013 lutang, CQ 2013 J, QZ 2011 ang, HX 2006 w, QJ 2007 Yang, LL 2016 Yang, UZ 2016 vang, LL 2016 vang, UZ 2006 ubtotal (95% CI) leterogeneity: Tau ² = 2.88; C est for overall effect. Z = 0.32 .2.114 d J, QZ 2011 ang, HX 2006 hou, YX 2007 hou, YX 207 hou, YX 207 hou, YX 207 hou, YX 207	229.58 194.58 192 210 191 199.7 206.7 210 :hi ² = 411.9 2 (P = 0.75) 192 210 191 206.7 210 191 206.7 210	78.8 11.58 11 700 11 24 70.1 70 7, df = 7 11 70 11 70 11 70 , df = 4 (f	31 200 30 60 30 50 50 481 (P < 0. 30 60 30 50 50 50 50 220 P < 0.0	240.55 225.68 155 202 180 190.4 205.3 202 00001); F 150 193 177 205 193 00001); F	10.84 10.84 13 74.2 13 25.8 71.2 74.2 74.2 74.2 74.2 74.2 74.2 72.9 12 70.8 72.9 12 70.8 72.9 = 94%	200 30 60 30 30 50 50 481 30 60 30 50 50 50 220	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	$\begin{array}{c} -0.13 \left[+0.83, 0.36 \right] \\ -2.77 \left[+3.04, -2.49 \right] \\ 3.03 \left[+2.68 \right] \\ 3.03 \left[+2.68 \right] \\ 0.11 \left[+0.25, 0.47 \right] \\ 0.21 \left[+0.37, 1.43 \right] \\ 0.37 \left[+0.14, 0.88 \right] \\ 0.22 \left[+0.37, 0.41 \right] \\ 0.11 \left[+0.28, 0.50 \right] \\ 0.19 \left[+0.96, 1.33 \right] \\ \end{array}$	
est for overall effect: Z = 0.31 .2.10 72 hr song, GH 2013 lutang, CQ 2013 1, QZ 2011 ang, HX 2006 u, QJ 2007 Yang, LL 2016 Yang, LL 2016 Yang, LL 2016 Yang, LL 2016 ubtotal (95% CD) leferogeneity. Tau ² = 2.88; C est for overall effect. Z = 0.32 .2.11 4 d 1, QZ 2011 ang, HX 2006 ubtotal (95% CD) leferogeneity. Tau ² = 0.87; C leferogeneity. Tau ² = 0.87; C	229.58 194.59 192 210 191 199.7 206.7 210 :hi ² = 411.9 2 (P = 0.75) 192 210 :hi ² = 68.38, 7 (P = 0.02)	78.8 11.58 11 70 7, df = 7 11 70 7, df = 7 11 70,1	31 200 30 60 30 50 50 50 481 (P < 0. 30 60 30 50 50 220 P < 0.0	240.55 225.68 155 202 190.4 205.3 202 200001); F 150 193 177 205 193 107 205 193	10.84 13 74.2 13 74.2 74.2 74.2 74.2 74.2 74.2 74.2 74.2	200 30 60 30 30 50 50 481 30 60 30 50 50 220 30 220	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	$\begin{array}{c} -0.13 \left[+0.83, 0.36 \right] \\ -2.77 \left[+3.04, -2.49 \right] \\ 3.03 \left[+2.68, 3.78 \right] \\ 0.11 \left[+0.25, 0.47 \right] \\ 0.9 \left[0.37, 1.43 \right] \\ 0.37 \left[+0.14, 0.88 \right] \\ 0.27 \left[+0.37, 0.41 \right] \\ 0.11 \left[+0.28, 0.50 \right] \\ 0.19 \left[-0.96, 1.33 \right] \\ \end{array}$	
est nor overail effect: $Z = 0.31$.2.10 72 hr iong, GH 2013 ituang, CG 2013 i, G2 2011 i, G2 2011 itutotal (95% C) itelerogeneity: Tau ² = 0.87; C itelerogeneity: Tau ² = 0.27; C itelerogenei	229.58 194.58 192 210 191 199.7 206.7 210 :hi ² = 411.9; 2 (P = 0.75) 192 210 191 206.7 210 192 210 191 206.7 210 192 210 192 210	78.8 11.58 11. 70 11 24 70.1 70 7, df = 7 11 70, 1 70, 1 70, 1 10, 1 70,	31 200 30 60 30 50 50 481 (P < 0. 30 60 50 50 50 50 50 50 50 50 50 50 50 50 50	240.55 225.68 155 202 190.4 205.3 202 00001); F 150 193 177 205 193 177 205 193 177 205 193 177 205	10.84 10.84 13 74.2 13 25.8 71.2 74.2 *= 98% 12 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9	200 30 60 30 50 50 50 481 30 60 30 50 50 220 30 50 50 50 50 50 50 50 50 50 5	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49] 3.03 [-26, 3.78] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.26 [-0.37, 0.41] 0.11 [-0.26, 0.50] 0.19 [-0.96, 1.33] 3.60 [2.76, 4.44] 0.24 [-0.12, 0.60] 1.20 [0.66, 1.75] 0.02 [-0.37, 0.42] 0.24 [-0.12, 0.60] 0.29 [0.74, 1.84] 3.84 [2.97, 4.71] 0.33 [-0.03, 0.69]	
est nor overail effect: $Z = 0.31$ 2.10 72 hr ong, GH 2013 tuang, CG 2013 1, OZ 2011 ong, HX 2006 u, GJ 2007 fang, LL 2016 fang, QP 2006 hubtotal (95% CD) leterogeneity: Tau ² = 2.68; C est for overail effect: Z = 0.32 2.114 d 1, OZ 2011 ong, HX 2006 hou, YX 2006 tubtotal (95% CD) leterogeneity: Tau ² = 0.87; C est for overail effect: Z = 2.21 2.12 5 d 1, OZ 2011 ong, HX 2006 hou, YX 2006 tubtotal (95% CD) leterogeneity: Tau ² = 0.87; C est for overail effect: Z = 2.21 2.12 5 d 1, OZ 2017	229.58 194.58 192.210 199.7 206.7 210 199.7 206.7 210 191 206.7 210 191 206.7 210 191 206.7 210 191 206.7 210 191 200.7 5 192 210 191 206.7 210 192 210 192 210 192 210 192 210 192 210 192 210 192 210 192 210 192 210 192 210 192 210 199.7 206.7 207.5 192 210 199.7 206.7 207.5 192.7 207.5 192.7 207.5	78.8 11.58 11 70 11 24 70.1 70 7, df = 7 71 70 11 70, 11 70, df = 4 (t 11 70 11	31 2000 300 300 50 50 481 (P < 0. 300 50 50 50 220 P < 0.0 30 30 30 30 30 30 30 30 30 30 30 30 30	240.55 225.68 155 202 180 190.4 205.3 202 000001); F 160 193 177 205 193 00001); F 143 187 175	10.84 13 13 74.2 13 25.8 71.2 74.2 74.2 *= 98% 12 72.9 12 70.8 72.9 = 94% 14 68.2 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 71.2 70.8 71.2 70.8 71.2 70.8 70.8 70.8 70.8 70.8 70.8 70.8 70.8	200 30 60 30 50 50 50 50 481 30 60 30 50 50 50 50 50 50 50 50 50 5	1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	$\begin{array}{r} -0.13 \left[+0.63, 0.36\right]\\ -2.77 \left[+3.04, -2.49\right]\\ 3.03 \left[+2.68, 3.78\right]\\ 0.11 \left[+0.25, 0.47\right]\\ 0.87 \left[+0.14, 0.88\right]\\ 0.22 \left[+0.37, 0.41\right]\\ 0.37 \left[+0.14, 0.88\right]\\ 0.22 \left[+0.37, 0.41\right]\\ 0.11 \left[+0.26, 0.50\right]\\ 0.19 \left[+0.96, 1.33\right]\\ \end{array}$	
est nor overail effect: $Z = 0.31$ 2.10 72 hr ong, GH 2013 luang, CG 2013 i, GZ 2011 i, GZ 2011 i, GZ 2011 i, GZ 2011 i, GZ 2011 i, GZ 2011 i, GZ 2015 hou, YX 2006 uitotal (95% CI) leterogeneity. Tau ² = 2.88; C est for overail effect: $Z = 0.32$ 2.11 4 d i, GZ 2011 ong, HX 2006 uitotal (95% CI) leterogeneity. Tau ² = 0.87; C est for overail effect: $Z = 2.22$ 2.12 5 d i, GZ 2011 ong, HX 2006 uitotal (95% CI) leterogeneity. Tau ² = 0.87; C est for overail effect: $Z = 2.22$ 2.12 5 d i, GZ 2011 ong, HX 2006 u, GJ 2007 i, GZ 2011 ong, HX 2006 u, GJ 2007 i, GZ 2011 ong, HX 2006 u, GJ 2007 i, GZ 20	229.58 194.58 192 210 191 199.7 206.7 210 2(P = 0.75) 2(P = 0.75) 2(P = 0.75) 191 206.7 7 (P = 0.02) 192 210 191 206.7	78.8 11.58 11.59 70 11 70.1 70.7 7, df = 7 7, df = 7 70 11 70.1 70 11 70.1 70 11 70.1	31 2000 300 300 500 500 500 500 500	240.55 225.68 155 202 180 190.4 205.3 202 00001); F 150 193 177 205 193 0001); F 143 187 187 175 204.1	10.84 13 74.2 13 25.8 71.2 74.2 74.2 74.2 74.2 72.9 12 72.9 12 72.9 12 72.9 12 72.9 12 72.9 12 72.9 12 72.9 12 72.9 12 72.9 12 70.8 4 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8 8	200 30 60 30 50 50 50 481 30 60 30 50 50 50 50 50 50 50 50 50 5	1.5% 1.5% 1.3% 1.5% 1.5% 1.5% 1.5% 1.5% 1.4% 1.5% 7.3%	$\begin{array}{c} -0.13 \left[-0.83, 0.36\right] \\ -2.77 \left[+3.04, -2.49\right] \\ 3.03 \left[+2.68, 3.78\right] \\ 0.11 \left[+0.25, 0.47\right] \\ 0.9 \left[0.37, 1.43\right] \\ 0.37 \left[+0.14, 0.88\right] \\ 0.27 \left[+0.37, 0.41\right] \\ 0.11 \left[+0.28, 0.50\right] \\ 0.19 \left[-0.96, 1.33\right] \\ \end{array}$	
ses ior overall effect: Z = 0.31 2.10 72 hr ong, CH 2013 ueng, Co 2013 org, CH 2013 ueng, Co 2013 org, LL 2018 ang, LL 20	229.58 194.58 192.58 192 210 191 199.7 206.7 210 :hi ² = 411.9; 2 (P = 0.75) 192 210 :hi ² = 68.38, 7 (P = 0.02) 192 210 191 206.7 210	78.8 11.58 11 70 11 70 70 7, df= 7 11 70 11 70 , df= 4 0 11 11 70 1 11 70 70 70 70 70 70 70 70 70 70 70 70 70	31 2000 30 60 30 50 50 481 (P < 0. 30 50 50 50 50 50 50 50 50 50 50 50 50 50	240,55 225,68 155 2022 180 190,4 205,3 202 200001); F 190,4 205,3 202 200001); F 193 193 193 193 193 193 193 193 205 193 193 205 193 193 205 190,4 193 193 193 193 193 193 193 193 193 193	*************************************	200 30 60 30 50 50 50 50 50 50 50 50 50 5	1.5% 1.5% 1.3% 1.5% 1.5% 1.5% 1.5% 1.5% 1.4% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5%	-0.13 [-0.63, 0.36] -2.77 [-3.04, -2.49] 3.03 [-26, 3.78] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.26 [-0.37, 0.41] 0.11 [-0.26, 0.50] 0.19 [-0.96, 1.33] 3.60 [2.76, 4.44] 0.24 [-0.12, 0.60] 1.20 [0.65, 1.75] 0.02 [-0.37, 0.42] 0.24 [-0.16, 0.63] 0.29 [0.74, 1.84] 3.84 [2.97, 4.71] 0.33 [-0.03, 0.69] 1.25 [0.70, 1.61] 0.34 [-0.03, 0.69] 1.25 [0.70, 1.61] 0.34 [-0.03, 0.69] 1.25 [0.70, 1.61] 0.34 [-0.03, 0.69]	
est nor overall effect: $Z = 0.31$ 2.10 72 hr ong, GH 2013 luang, CG 2013 i, QZ 2011 ang, HX 2006 u, QJ 2007 fang, LL 2018 fang, QP 2006 ubtotal (95% CD) eterogeneity. Tau ² = 2.68; C est for overall effect: $Z = 0.32$ 2.114 d i, QZ 2011 ong, HX 2006 u, QJ 2007 fang, QP 2006 hou, YX 2006 u, QJ 2007 fang, QP 2006 hou, YX 2006 u, QJ 2007 fang, QP 2006 ang, QP 2006 ist for overall effect: $Z = 2.27$ 2.125 d , QZ 2011 ong, HX 2006 u, QJ 2007 fang, QP 2006 ist for overall effect: $Z = 2.27$ J, QZ 2011 ong, HX 2006 u, QJ 2007 fang, QP 2006 butotal (95% CD) eterogeneity. Tau ² = 0.97; C eterogeneity. Tau ² = 0.07; C	229.58 194.58 192.58 192 210 191 199.7 206.7 210 :hi ² = 411.93 2 (P = 0.75) 192 210 :hi ² = 68.39, 7 (P = 0.02) 191 206.7 210 	78.8 11.58 11 70 11 70 70.1 70 7, df = 7 11 70.1 70 11 70 11 70 11 70 11 70 11 70 11 70 11 70 4f = 4 7 0 11 70 11 70 70 11 70 70 70 11 70 70 70 70 70 70 70 70 70 70 70 70 70	31 2000 30 30 50 50 481 (P < 0. 30 50 50 50 50 50 50 50 50 50 50 50 50 50	240.55 225.68 155 2022 180 190.4 205.3 202 2000001); F 150 190.4 205 202 202 2000001); F 150 193 202 205 193 205 193 205 193 205 193 205 193 205 193 205 193 205 193 205 193 205 193 205 193 205 205 205 205 205 205 205 205 205 205	sz 10.84 11.84 13 74.2 13 25.8 71.2 74.2 74.2 74.2 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 71.2 70.8 71.2 70.8 74.2 70.8 74.2 70.8 74.2 70.8 74.2 70.8 74.2 74.2 70.8 74.2 70.8 74.2 70.8 74.2 70.8 74.2 70.8	200 30 60 30 50 50 50 50 50 50 50 50 50 5	1.5% 1.3% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5	$\begin{array}{r} -0.13 \left[+0.63, 0.36\right]\\ -2.77 \left[+3.04, -2.49\right]\\ 3.03 \left[+2.68, 3.78\right]\\ 0.11 \left[+0.25, 0.47\right]\\ 0.91 \left[+3.77, 1.43\right]\\ 0.37 \left[+0.14, 0.88\right]\\ 0.22 \left[+0.37, 0.41\right]\\ 0.11 \left[+0.26, 0.50\right]\\ 0.19 \left[+0.96, 1.53\right]\\ 3.60 \left[+2.76, 4.44\right]\\ 0.24 \left[+0.12, 0.60\right]\\ 1.20 \left[+0.36, 1.75\right]\\ 0.22 \left[+0.37, 0.42\right]\\ 0.24 \left[+0.12, 0.63\right]\\ 0.29 \left[0.14, 1.94\right]\\ 3.84 \left[+2.97, 4.71\right]\\ 0.33 \left[+0.03, 0.69\right]\\ 1.25 \left[0.37, 0.41\right]\\ 0.44 \left[+0.36, 0.43\right]\\ 0.33 \left[+0.03, 0.69\right]\\ 1.25 \left[0.70, 1.81\right]\\ 0.44 \left[+0.36, 0.43\right]\\ 0.33 \left[+0.06, 0.73\right]\\ 1.08 \left[0.21, 1.94\right]\\ \end{array}$	
ess ror overall effect: Z = 0.31 2.10 72 hr ong, CH 2013 ueng, CO 2013 (02 2011 i, 02 2011 i, 02 2011 i, 02 2011 i, 02 2011 i, 02 2015 inng, LL 2016 inng, LL 2016 inng, LL 2016 inng, LL 2016 iest for overall effect Z = 0.33 2.114 4 i, 02 2017 inng, CH 2006 ubtotal (95% C) efforgeneity: Tau ² = 0.87; C 2.12 5 d i, 0.2 2011 inng, LH 2006 ubtotal (95% C) efforgeneity: Tau ² = 0.87; C 2.12 5 d i, 0.2 2007 inng, QH 2005 inng,	$\begin{array}{c} 229.58\\ 194.58\\ 194.58\\ 192\\ 210\\ 191\\ 199.7\\ 210\\ 206.7\\ 210\\ 201\\ 191\\ 206.7\\ 210\\ 191\\ 200\\ 191\\ 200\\ 191\\ 200\\ 7 (P=0.02)\\ 191\\ 200\\ 7 (P=0.02)\\ 192\\ 210\\ 191\\ 200\\ 100\\ 100\\ 100\\ 100\\ 100\\ 100\\ 10$	78.8 11.58 11 70 11 24 70.1 70 7, df = 7 7 11 70.1 70 7 11 70.1 70 11 70, df = 4 (0 , df = 4 (0 , df = 4 (0 , df = 4 7 0	31 200 30 30 30 50 50 50 60 30 60 30 60 50 50 50 50 50 50 50 80 30 80 80 80 80 80 80 80 80 80 80 80 80 80	240,55 225,68 155 2022 180 190,4 205,3 202 202 2000001); F 150 193 202 202 2000001); F 143 187 177 205 193 205 193 2041 187 187 187 187 205 193 2041 187 187 187 205 180 190,4 205 205 205 205 202 205 202 205 202 205 202 205 202 205 202 205 202 205 202 205 202 205 202 202	82 10.84 11.84 13 74.2 13 25.8 71.2 74.2 74.2 74.2 70.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 72.9 12 70.8 74.2 70.8 74.2 74.2 75.8 74.2 74.2 75.8 74.2 74.2 75.8 74.2 74.2 75.8 74.2 74.2 75.8 74.2 75.8 74.2 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 74.2 75.8 75.	200 30 60 30 50 50 481 30 60 30 50 220 30 60 30 50 220 220	1.5% 1.3% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5	-0.13 [-0.83, 0.36] -2.77 [-3.04, -2.49] 3.03 [2.26, 3.78] 0.11 [-0.25, 0.47] 0.90 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.02 [-0.37, 0.41] 0.11 [-0.26, 0.50] 0.19 [-0.96, 1.33] 3.60 [2.76, 4.44] 0.24 [-0.36, 1.20 80] 1.20 [0.85, 1.75] 0.22 [-0.37, 0.42] 0.24 [-0.16, 0.63] 0.39 [0.14, 1.84] 3.84 [2.97, 4.71] 0.33 [-0.03, 0.69] 1.26 [0.70, 1.81] 0.34 [-0.6, 0.73] 0.34 [0.6, 7.73] 0.34 [0.6, 7.73] 1.08 [0.21, 1.94]	
ess nor overall effect: Z = 0.31 2.10 72 hr ong, GH 2013 ueng, CO 2013 j, OZ 2011 ueng, CO 2013 j, OZ 2011 ing, LL 2016 ing, LL 2016 ing, LL 2016 ing, GP 2006 out, VX 2006 lubtotal (95% C) elerogeneity: Tau ² = 0.87; C elerogeneity: Tau ² = 0.87; C ist for overall effect: Z = 2.21 2.12 4 (J, Z 2011 ong, HZ 2006 ubtotal (95% C) elerogeneity: Tau ² = 0.87; C ist for overall effect: Z = 2.21 2.12 5 d ist for overall effect: Z = 2.42 st for overall effect: Z = 2.43 st f	$\begin{array}{c} 229.58\\ 194.59\\ 194.59\\ 192\\ 210\\ 191\\ 199.7\\ 210\\ 206.7\\ 210\\ 210\\ 210\\ 210\\ 192\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 206.7\\ 210\\ 191\\ 200.7\\ 210\\ 210\\ 191\\ 200.7\\ 210\\ 210\\ 210\\ 200.7\\ 210\\ 210\\ 200.7\\ 210\\ 200.7\\ 200.7\\ 200\\ 200\\ 200\\ 200\\ 200\\ 200\\ 200\\ 20$	78.8 11.58 11 70 11 24 70.1 70 7, df = 7 7 11 70.1 70 7 11 70.1 70 11 70.1 70 0 11 70, df = 4 (0 11 70, df = 4 7 0 11 70, df = 7 7 0 11 70 70 70 70 70 70 70 70 70 70 70 70 70	31 200 30 30 30 50 50 50 50 50 50 50 50 220 P < 0.0 30 30 60 30 30 50 50 50 50 50 50 50 50 50 720 9 220 P < 0.0 30 30 30 30 30 30 30 30 30 30 30 30 30	240,55 20225,68 155 202 205,3 180 190,4 205,3 202 202 202 2000001); F 150 193 193 193 193 193 193 193 193 193 193	32 32 32 32 32 32 32 32 32 32	200 30 60 30 50 50 481 30 60 50 220 30 60 30 50 220 30 50 50 220 30 50 50 50 50 50 50 50 50 50 5	1.5% 1.3% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5% 1.5	-0.13 [-0.83, 0.36] -2.77 [-3.04, -2.49] 3.03 [2.26, 3.78] 0.11 [-0.25, 0.47] 0.9 [0.37, 1.43] 0.37 [-0.14, 0.88] 0.22 [-0.37, 0.41] 0.11 [-0.26, 0.50] 0.19 [-0.96, 1.33] 3.50 [2.76, 4.44] 0.24 [-0.32, 0.60] 1.20 [0.85, 1.75] 0.22 [-0.37, 0.42] 0.24 [-0.32, 0.60] 1.20 [0.85, 1.75] 0.22 [-0.37, 0.42] 3.84 [2.97, 4.71] 0.33 [-0.03, 0.69] 1.26 [0.70, 1.81] 0.44 [-0.36, 0.43] 0.33 [-0.06, 0.73] 1.06 [0.27, 0.54]	

Fig. 3. Forest plot of store effect on PLt count under 4 °C. 19 studies (7549 samples) under 4 °C measured PLt count. Storage at 4 °C showed much more stability than at RT. Except 8 h., there were no statistically significant changes up to 3 d but changed at 4 d.

Study or Subgroup	Contr Mean S	al D Total	Experiment Mean SD	al Total	SI	d. Mean Difference IV, Random, 95% Cl	Std. Mean Difference IV, Random, 95% Cl
4.1.1 15 min Chen, C 2004 Dong, LM 2014 Han, JP 2015 Jin, LY 2011 Wang, Y 2009 Subtotal (95% CI)	4.47 0.5 4.6 1 4.5 1 4.26 0.6 4.47 0.5	6 40 2 200 8 50 9 30 6 40 360	4.46 0.58 4.9 1.5 4.5 1.9 4.27 0.69 4.46 0.58	40 200 50 30 40 360	0.8% 0.9% 0.8% 0.7% 0.8% 4.0%	0.02 [-0.42, 0.46] -0.22 [-0.42, -0.02] 0.00 [-0.39, 0.39] -0.01 [-0.52, 0.49] 0.02 [-0.42, 0.46] -0.12 [-0.27, 0.03]	•
Heterogeneity: Tau* = 0.00; Cl Test for overall effect: Z = 1.60 4.1.2 30 min Chen, C 2004	4.47 0.5	= 4 (P = 0.	.68); i*= 0% 4.48 0.58	40	0.8%	-0.02 [-0.46, 0.42]	_
Han, JP 2015 Jin, LY 2011 Wang, Y 2009 Yu, SQ 2003 Zhou, YJ 2013 Subtotal (65% CI)	4.5 1 4.26 0.8 4.47 0.5 3.94 0.5 4.07 0.3	8 50 9 30 8 40 5 60 4 40 260	4.5 0.9 4.28 0.72 4.48 0.58 4.07 0.61 4.06 0.63	50 30 40 60 40 260	0.8% 0.7% 0.8% 0.8% 0.8% 4.7%	-0.08 [-0.47, 0.32] -0.03 [-0.53, 0.48] -0.02 [-0.46, 0.42] -0.22 [-0.58, 0.14] 0.01 [-0.42, 0.45] -0.07 [-0.24, 0.10]	-
Test for overall effect: Z = 0.82	(P = 0.41)	• 5 (P = 0.	.00), I* = 0%				
4.1.3 1 br Al, WJ 2015 Dong, LM 2014 Han, JP 2015 Huang, SF 2014 Jiang, RR 2013 LI, QZ 2011 Lia W 2015	5.4 1.1 4.6 1 4.5 1 3.8 0.2 4.71 0.8 4.32 0.0 4.86 0	4 82 2 200 6 50 4 160 5 30 6 30 2 136	5.37 1.14 4.8 1.3 4.7 0.5 3.77 0.26 4.73 0.65 4.33 0.05 4.68 0.18	82 200 50 160 30 30	0.9% 0.9% 0.9% 0.9% 0.7% 0.7%	0.03 [-0.28, 0.33] -0.16 [-0.36, 0.04] -0.17 [-0.56, 0.23] 0.12 [-0.10, 0.34] -0.03 [-0.54, 0.48] -0.18 [-0.69, 0.33] -0.10 [-0.54, 0.13]	
Gian, M 2011 Tan, FS 2011 Wang, YO 2014 Subtotal (95% Cl) Heterogeneily: Tau*= 0.03; Cl	4.79 0.66 4.88 0.4 5.03 0.1	8 15 5 35 1 30 768 r= 9 (P = 1	4.89 0.468 4.66 0.36 4.92 0.1 0.02); P= 55%	15 35 30 768	0.6% 0.8% 0.7% 7.9%	-0.17 [-0.89, 0.55] 0.05 [-0.42, 0.52] 1.03 [0.49, 1.57] 0.01 [-0.15, 0.18]	
4.1.4 1.5 hr	(P=0.86)						
Chen, C 2004 Jin, LY 2011 Wiang, Y 2009 Zhou, YJ 2013 Subtotal (95% CI) Heterogeneity. Tau ² = 0.00; CI Test for overall effect. Z = 0.51	4.47 0.5 4.26 0.6 4.47 0.5 4.07 0.7 hi ^p = 0.06, df (P = 0.61)	6 40 9 30 6 40 4 40 150 = 3 (P = 1.	4.49 0.6 4.33 0.73 4.49 0.8 4.13 0.72 .00); P= 0%	40 30 40 40 150	0.8% 0.7% 0.8% 0.8% 3.1%	-0.03 [-0.47, 0.40] -0.10 [-0.60, 0.41] -0.03 [-0.47, 0.40] -0.08 [-0.52, 0.36] -0.06 [-0.29, 0.17]	ŧ
4.1.5 2 hr AL WL 2015	54 11	4 82	6.33 1.12	82	0.9%	0.06 (-0.24, 0.37)	_
Gong, QH 2013 Han, JP 2015	4.48 0.8	1 60 6 50	4.47 0.62 5 0.9	60 50	0.8%	0.02 [-0.34, 0.37] -0.38 [-0.78, 0.01]	-
Huang, SF 2014 LI, OZ 2011	3.8 0.1 4.32 0.0	4 160	3.75 0.24 4.3 0.05 4.29 0.22	160 30	0.9%	0.21 [-0.01, 0.43] 0.36 [-0.15, 0.87]	E-
Liang, Q 2004 Qian, M 2011	3.79 0.7	4 40	4.29 0.33 3.79 0.74 4.89 0.569	40	0.8%	-0.06 [-0.28, 0.16] 0.00 [-0.44, 0.44] -0.16 [-0.87, 0.56]	+
Sun, DJ 2015 Tan, FS 2011	4.58 0.4	2 160	4.4 1.2 4.67 0.4	160	0.9%	-0.12 [-0.34, 0.10] 0.02 [-0.45, 0.49]	+
Wang, YG 2014 Wei, SJ 2016	5.03 0.1 4.1 1	1 30 6 71	4.9 0.11 4.8 1.2	30 71	0.7%	1.17 [0.62, 1.72] -0.49 [-0.83, -0.16]	
Zou, HY 2006 Subtotal (95% CI)	4.3 0	1 70 1473	4.5 0.2	70 1363	0.8%	-1.26 [-1.62, -0.89] -0.08 [-0.26, 0.10]	- •
Test for overall effect: Z = 0.90	n ^a = 83.50, d (P = 0.37)	15 (P ² 4	0.00001); (*=)	81%			
4.1.6 3 m Daves, M 2015 Dong, LM 2014	3.64 0.1 4.6 1	6 16 2 200	3.66 0.75 4.5 1.1	16 200	0.6%	-0.03 [-0.72, 0.67] 0.09 [-0.11, 0.28]	+
Han, JP 2015 Li, OZ 2011 Liu, W 2015	4.5 1 4.32 0.0 4.66 0	6 50 6 30 2 136	5.2 1.3 4.31 0.05 4.65 0.17	50 30 136	0.8%	-0.48 [-0.87, -0.08] 0.18 [-0.33, 0.69] 0.05 [-0.18, 0.29]	
Zhou, YJ 2008 Zhou, YJ 2013 Subtotal (95% CI)	4.31 0.3	5 10 4 40 482	4.3 0.2 4.18 0.89	40 482	0.5% 0.8% 5.2%	-0.13 [-0.57, 0.31] -0.01 [-0.17, 0.14]	-
Heterogeneity: Tau* = 0.01; Cl Test for overall effect: Z = 0.18	hi ^a = 7.30, df (P = 0.86)	= 6 (P = 0.	29); P=18%				
4.1.7 4 hr Al, WJ 2015 Gong, QH 2013	5.4 1.1 4.48 0.6	4 82 1 60	5.29 1.11 4.47 0.6	82 60	0.9%	0.10 [-0.21, 0.40] 0.02 [-0.34, 0.37]	+
Hu, HY 2015 Huang, CQ 2013 Huang, SF 2014	4.43 1.4 3.85 0.5 3.8 0.3	2 160 4 200 4 160	5.08 1.12 3.84 0.48 3.7 0.28	30 200 160	0.8%	-0.47 [-0.86, -0.08] 0.02 [-0.18, 0.22] 0.38 [0.16, 0.60]	
Jiang, RR 2013 LI, QZ 2011 LI, YF 2015	4.71 0.8 4.32 0.0 4.27 0.3	5 30 6 30 5 160	4.73 0.65 4.32 0.06 4.31 0.31	30 30 160	0.7% 0.7% 0.9%	-0.03 [-0.54, 0.48] 0.00 [-0.51, 0.51] -0.12 [-0.34, 0.10]	-
Liang, Q 2004 Qian, M 2011 Rui, F 2015	3.79 0.1 4.79 0.68 4.6 1	4 40 8 15 2 120	3.78 0.74 4.89 0.569 5.1 1	40 15 120	0.8% 0.6% 0.9%	0.01 [-0.42, 0.45] -0.16 [-0.87, 0.56] -0.45 [-0.71, -0.19]	-
Sun, DJ 2015 Tan, FS 2011 Wang, J 2016	4.3 0 4.58 0.4 4.28 1.3	2 160 5 35 4 200	5.1 0.7 4.66 0.48 4.67 1.39	160 35 200	0.9% 0.8% 0.9%	-1.55 [-1.80, -1.30] 0.04 [-0.43, 0.51] -0.29 [-0.48, -0.09]	
Wang, LL 2016 Wang, YG 2014 Wei, SJ 2016	5.14 1.0 5.03 0.1 4.1 1	6 30 1 30 6 71	5.1 0.96 4.89 0.15 5.3 1.3	30 30 71	0.7% 0.7% 0.8%	0.04 [-0.47, 0.55] 1.05 [0.51, 1.59] -0.82 [-1.16, -0.48]	_T-
Wu, YY 2006 Yu, SQ 2003 Zou, HY 2016	5.07 0.8 3.94 0.4 4.3 0	9 30 5 60 1 70	4.86 0.51 4.01 0.57 5.1 0.3	30 60 70	0.7% 0.8% 0.7%	0.34 [-0.17, 0.85] -0.12 [-0.48, 0.23] -3.56 [-4.10, -3.02]	- Ŧ
Subtotal (95% CI) Heterogeneity: Tau ^a = 0.46; CI Test for overall effect: Z = 1.75	hi ^a = 344.44, (P = 0.08)	1743 sf = 19 (P	< 0.00001); (*=	1613 94%	16.0%	-0.28 [-0.59, 0.03]	•
4.1.8 6 hr Al, WJ 2015	5.4 1.1	4 82	6.28 1.11	82	0.9%	0.11 [-0.20, 0.41]	
Daves, M 2015 Dong, LM 2014 LI, YF 2015	3.64 0.7 4.6 1 4.27 0.3	6 16 2 200 5 160	3.68 0.77 4.9 1.3 4.37 0.37	16 200 160	0.6% 0.9% 0.9%	-0.05 [-0.74, 0.64] -0.24 [-0.44, -0.04] -0.28 [-0.50, -0.06]	=
Liang, Q 2004 Liu, W 2015 Sun, DJ 2015	3.79 0.1 4.66 0 4.3 0	4 40 2 136 2 160	3.78 0.74 4.7 0.19 5.8 1.3	40 136 160	0.8% 0.9% 0.9%	0.01 [-0.42, 0.45] -0.20 [-0.44, 0.03] -1.61 [-1.86, -1.36]	- 1
Tan, FS 2011 Wang, J 2016 Wang, LL 2016	4.68 0.4 4.28 1.3 5.14 1.0	5 35 4 200 6 30	4.67 0.54 4.91 1.47 5.06 0.87	35 200 30	0.8%	0.02 [-0.45, 0.49] -0.45 [-0.85, -0.25] 0.08 [-0.42, 0.59]	
Wang, YO 2014 Wen, XM 2008 Wu, YY 2006	5.03 0.1 4.31 0.2 5.07 0.6	1 30 5 10 9 30	4.92 0.1 4.34 0.22 4.95 0.48	30 10 30	0.7% 0.5% 0.7%	1.03 [0.49, 1.57] -0.12 [-1.00, 0.78] 0.20 [-0.31, 0.71]	
Subtotal (95% Cl) Heterogeneity: Tau ^a = 0.29; Cl Test for overall effect. Z = 0.89	hi ^a = 146.24, (P = 0.37)	1129 ff = 12 (P	< 0.00001); (*=	92%	10.2%	-0.14 [-0.46, 0.17]	1
4.1.9 8 hr Al, WJ 2015	5.4 1.1	4 82	6.26 1.1	82	0.9%	0.12 [-0.18, 0.43]	_
Geng, GH 2013 Huang, SF 2014 Jiang, RR 2013	4.48 0.8 3.8 0.2 4.71 0.6	4 160 5 30	4.46 0.67 3.76 0.3 4.73 0.66	160 30	0.8%	0.03 [-0.33, 0.39] 0.15 [-0.07, 0.37] -0.03 [-0.54, 0.48]	<u> </u>
Li, 02 2011 Li, YF 2015 Qian, M 2011	4.32 0.0 4.27 0.1 4.79 0.68	6 30 5 160 8 15	4.33 0.06 4.35 0.35 4.91 0.582	30 160 15	0.9%	-0.16 [-0.87, 0.34] -0.23 [-0.45, -0.01] -0.19 [-0.90, 0.53]	
Wang, LL 2016 Wang, YG 2014	5.14 1.0 5.03 0.1	5 35 6 30 1 30	4.00 0.40 5.03 0.88 4.82 0.19	30 30	0.7%	0.04 [-0.43, 0.51] 0.11 [-0.40, 0.62] 1.34 [0.77, 1.90]	±—
Subtotal (95% CI) Heterogeneity: Tau ² = 0.07; CI Test for overall effect. 7 = 0.99	hi ² = 28.59, d	662 = 10 (P =	0.001); I ^a = 85	662 %	8.5%	0.10 [-0.10, 0.30]	t
4.1.10 12 hr	54 11	4 87	52 1.08	87	0.9%	0184013.049	_
Dong, LM 2014 Huang, CQ 2013 Li, YF 2015	4.6 1 3.85 0.5 4.27 0.3	2 200 4 200 5 160	4.6 1.2 3.78 0.48 4.4 0.33	200 200 160	0.9%	0.00 [-0.20, 0.20] 0.14 [-0.06, 0.33] -0.38 [-0.60, -0.16]	
Rui, F 2015 Wang, YO 2014 Wu, YY 2006	4.6 1 5.03 0.1 5.07 0.6	2 120 1 30 9 30	4.39 0.33 4.94 0.09 4.82 0.53	120 30 30	0.9%	0.24 [-0.02, 0.49] 0.88 [0.35, 1.42] 0.40 [-0.11, 0.91]	<u> </u>
Subtotal (95% CI) Heterogeneity: Tau ^a = 0.07; CI Test for overall effect: Z = 1.26	ni [#] = 29.63, d	822 f= 6 (P < 1	0.0001); i*= 80*	822	5.9%	0.15 [-0.08, 0.38]	t
4.1.12 24 hr ALWU 2015	5.4 1.1	4 82	5.13 1.07	82	0.9%	0.24 (-0.06, 0.55)	_
Daves, M 2015 Dong, LM 2014 Gong, GH 2013	3.64 0.3 4.6 1 4.48 0.6	6 16 2 200 1 60	3.65 0.75 4.9 1.2 4.5 0.63	16 200 60	0.6% 0.9% 0.8%	-0.01 [-0.71, 0.68] -0.25 [-0.45, -0.05] -0.03 [-0.39, 0.33]	=
Huang, CQ 2013 Jiang, RR 2013 Li, QZ 2011	3.85 0.5 4.71 0.8 4.32 0.0	4 200 5 30 6 30	3.64 0.47 4.81 0.75 4.31 0.07	200 30 30	0.9% 0.7% 0.7%	0.41 [0.22, 0.61] -0.14 [-0.85, 0.37] 0.15 [-0.36, 0.66]	+
LI, YF 2015 Qian, M 2011 Wang, LL 2016	4.27 0.3 4.79 0.68 5.14 1.0	5 160 8 15 6 30	5.39 0.79 4.94 0.579 4.98 0.68	160 15 30	0.9% 0.6% 0.7%	-1.83 [-2.09, -1.57] -0.23 [-0.95, 0.48] 0.18 [-0.33, 0.68]	-+
Wang, YG 2014 Wood, B L. (health) 1999 Wood, B L. (patient) 1999	5.03 0.1 4.62 0.4 3.68 0.6	1 30 9 21 8 113	4.87 0.07 4.85 0.52 3.86 0.89	30 21 113	0.7% 0.7% 0.9%	1.71 [1.12, 2.31] -0.06 [-0.66, 0.55] 0.03 [-0.23, 0.29]	+
Yu, SQ 2003 Subtotal (95% CI) Heterogeneity: Tau ² = 0.53; CI	3.94 0.5	5 60 1047 sf = 13 (P	4.05 0.59	60 1047 95%	0.8%	-0.19 [-0.55, 0.17] -0.01 [-0.41, 0.38]	•
Test for overall effect: Z = 0.07 4.1.13 2 d	(P = 0.94)						
Al, WJ 2015 Gong, QH 2013 Huang, CQ 2013	5.4 1.1 4.48 0.8 3.85 0.4	4 82 1 60 4 200	5.05 1.07 4.56 0.66 3.6 0.45	82 60 200	0.9% 0.8% 0.9%	0.32 (0.01, 0.62) -0.13 (-0.48, 0.23) 0.50 (0.30, 0.70)	+
LI, QZ 2011 Qian, M 2011 Wang, LL 2016	4.32 0.0 4.79 0.68 5.14 1.0	6 30 8 15 6 30	4.3 0.08 4.99 0.577 4.88 0.58	30 15 30	0.7% 0.6% 0.7%	0.28 [-0.23, 0.79] -0.31 [-1.03, 0.41] 0.30 [-0.21, 0.81]	- ‡
Wang, YG 2014 Subtotal (95% CI) Heterogeneity: Tau ^e = 0.27: CI	5.03 0.1	1 30 447 = 6 (P < 1	4.82 0.05 0.00001); P = 8	30 447 8%	0.6% 5.3%	2.43 [1.75, 3.10] 0.45 [0.03, 0.88]	•
Test for overall effect: Z = 2.08 4.1.14 3 d	(P = 0.04)						
Al, WJ 2015 Gong, GH 2013 Huang, CQ 2013	5.4 1.1 4.48 0.8 3.85 0.5	4 82 1 60 4 200	4.96 1.03 4.54 0.67 3.55 0.42	82 60 200	0.9% 0.8% 0.9%	0.40 [0.09, 0.71] -0.09 [-0.45, 0.26] 0.62 [0.42, 0.82]	+-
Li, QZ 2011 Wang, LL 2016 Wang, YG 2014	4.32 0.0 5.14 1.0 5.03 0.1	6 30 6 30 1 30	4.28 0.1 4.78 0.63 4.79 0.09	30 30 30	0.7% 0.7% 0.6%	0.48 [-0.03, 0.99] 0.41 [-0.10, 0.92] 2.36 [1.69, 3.03]	Ē.—
Subtotal (95% Cl) Heterogeneity: Tau ^a = 0.26; Cl Test for overall effect: Z = 2.82	hi ^e = 41.99, d (P = 0.005)	432 1= 5 (P < 1	0.00001); I ^a = 8	432 8%	4.7%	0.64 [0.19, 1.08]	•
Total (95% CI) Heterogeneity: Tau ^a = 0.23; CI Test for overall effect: Z = 0.10	hi ^a = 1187.71 (P = 0.92)	9775 df = 126	(P < 0.00001);	9535 P= 89%	100.0%	-0.00 [-0.10, 0.09] +	Francisco Francisco

3.4. Sensitivity Analysis and Publication Bias

Except HCT 4 °C 2 d, MCHC 4 °C 8 h., AST RT 24 h. and TP RT 24 h., sensitive analysis results were consistent (S Table 1), which indicates our results are stable and reliable. Egger test was applied to test publication bias. By trim and fill method, both the results of fixed and random effects model are just the same with original result (Appendix 2, Fig. S28 for funnel plot for trim-and-fill method).

4. Discussion

Several lines of evidence attest that the vast of laboratory errors (70%) emerge from the pre-analytical phase rather than from the analytical and post-analytical phases (Lippi et al., 2006). In the pre-analytic phase, reliable specimen storage is fundamental to high-quality test results (Narayanan, 2000). Inappropriate storage conditions would pose a tangible challenge for the sample quality (Adcock et al., 2012)

The CBC or hemogram is a routine laboratory test that evaluates number, size, morphology and related indices of the blood: WBC, platelet and RBC. Significant time-and temperature-dependent changes can occur when the storage of blood is prolonged (Hedberg and Lehto, 2009; Jobes et al., 2011). Earlier studies have reported acceptable stability after 24 h. of storage for basic parameters, such as RBC count, WBC count and platelet count, HGB, MCH and MCHC (Lewis SM, 1975). More recently, different authors have reported that some measurements are stable up to 72 h. after collection if stored at 4 °C refrigerated (Ashenden et al., 2013; Robinson et al., 2011; Voss et al., 2008) and our results confirmed this. Storage time and temperature may have a small influence on WBC count. Although it hadn't analyzed in our study, there were studies reflect that WBC differential count was not stable over time (Hill et al., 2009). Although one study reported a better stability of the PLt count at room temperature (Imeri et al., 2008), we had no evidence to support this. Sample was stable after 2 d storage at 4 °C and RT. Four days at 4 °C had changed the PLt count which might be attributed to alterations in platelet morphology, movement and aggregation (Mahmoodi et al., 2006). Another parameter reflects the propriety of platelet is MPV. From our results, it changed at the first compared point-in-time (1 h.). The reliable MPV might have something to do with time- and concentration-related changes in platelet shape from discoid to spherical and swelling. Some red blood cell related parameters, such as RBC count, HGB, and MCHC, were less stable when stored at 4 °C, which may be affected by initial freezing followed by refrigeration (Lombardi et al., 2011). Those raise an important concern that refrigeration of specimens may not be satisfactory as previously believed. As the time gone, RBC has been shown to significantly drop because of hemolysis. Increased cell permeability would be found by the increment of MCV, an index reflected to the swelling of the RBC. The change in HCT and MCHC are clearly the consequence of change in MCV because those parameters are partially derived from MCV (Buoro et al., 2016; Daves et al., 2015; Gunawardena et al., 2017).

Parameters of CMP should also be considered for the time- and temperature- dependent change, although studies focused on this was relatively few. All in all, the reasons that may be responsible for change are as follows: firstly, self-consumption. Studies have found that blood glucose decrease by 5% ~ 7% (0.4 mmol/L) per hour after venipuncture because of erythrocyte glycolysis, WBC degeneration and contamination by bacteria (Gunawardena et al., 2017). What we could see was that even by 1 h. at RT, blood glucose showed a statistical difference. Secondly, increased permeability of blood cells, influencing Na, K, Cl, TBIL and

Fig. 4. Forest plot of store effect on RBC count under RT. We included 31 studies (19,310 samples) under RT in the RBC count meta-analysis. The sample was stable for 24 h. at RT.

284

D. Wu et al. / EBioMedicine 24 (2017) 277-285

	C	Control		Experimental				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% Cl	IV, Random, 95% Cl
11.2.2 2 hr									
Bian, S 2014	6.9	3.5	50	6.3	3.1	50	4.6%	0.18 [-0.21, 0.57]	+
Cui, LN 2016	6.82	3.65	50	6.72	3.62	50	4.6%	0.03 [-0.36, 0.42]	+
Deng, ZK 2012	6.82	3.6	30	6.61	3.7	30	4.4%	0.06 [-0.45, 0.56]	_
Gao, YH 2016	7	3.3	126	6.8	3.4	126	4.8%	0.06 [-0.19, 0.31]	+
Zhu, Q 2012	5.186	0.585	25	5.147	0.592	25	4.3%	0.07 [-0.49, 0.62]	- <u>+</u> -
Subtotal (95% CI)			281			281	22.7%	0.08 [-0.09, 0.24]	•
Heterogeneity: Tau ² =	0.00; C	hi² = 0.3	5, df =	4 (P = 0)	.99); l² =	: 0%			
Test for overall effect:	Z = 0.89	P = 0.3	37)						
11.2.6 12 hr									
Bian, S 2014	6.9	3.5	50	6.9	3.5	50	4.6%	0.00 [-0.39, 0.39]	
Cui, LN 2016	6.82	3.65	50	5.68	2.93	50	4.6%	0.34 [-0.05, 0.74]	+
Cui, QL 2012	5.2	1.1	5	5.2	0.5	5	3.0%	0.00 [-1.24, 1.24]	
Deng, ZK 2012	6.82	3.6	30	6.78	3.6	30	4.4%	0.01 [-0.50, 0.52]	
Gao, YH 2016	7	3.3	126	5.7	3.1	126	4.8%	0.40 [0.16, 0.65]	
Yan, F 2015	5.07	0.25	53	5.88	0.2	53	4.2%	-3.55 [-4.17, -2.93]	<u> </u>
Zeng, ZL 2007	5.12	0.3	30	5.02	0.33	30	4.4%	0.31 [-0.20, 0.82]	_
Subtotal (95% CI)			344			344	30.0%	-0.35 [-1.17, 0.48]	
Heterogeneity: Tau ² =	1.15; C	hi ² = 14'	1.15, d	f=6(P	< 0.0000	01); l ² =	96%		
Test for overall effect:	Z = 0.82	P = 0.4	41)						
11.2.7 24 hr									
Bian, S 2014	6.9	3.5	50	6.9	3.7	50	4.6%	0.00 [-0.39, 0.39]	
Cui, LN 2016	6.82	3.65	50	5.01	2.57	50	4.6%	0.57 [0.17, 0.97]	
Cui, QL 2012	5.2	1.1	5	5	0.4	5	3.0%	0.22 [-1.03, 1.46]	
Deng, ZK 2012	6.82	3.6	30	6.88	3.8	30	4.4%	-0.02 [-0.52, 0.49]	
Gao, YH 2016	7	3.3	126	5	3.3	126	4.8%	0.60 [0.35, 0.86]	-
Yan, F 2015	5.07	0.25	53	6.33	0.35	53	4.1%	-4.11 [-4.79, -3.43]	
Yang, YM 2015	4.98	0.7	30	5.05	0.81	90	4.6%	-0.09 [-0.50, 0.32]	
Zeng, ZL 2007	5.12	0.3	30	4.97	0.35	30	4.4%	0.45 [-0.06, 0.97]	+
Zhang, TY 2014	5.2	0.2	10	5.1	0.2	10	3.7%	0.48 [-0.41, 1.37]	
Zheng, HF 2016	5.2	0.3	120	5	0.2	120	4.8%	0.78 [0.52, 1.04]	
Zhu, Q 2012	5.186	0.585	25	5.125	0.568	25	4.3%	0.10 [-0.45, 0.66]	
Subtotal (95% CI)			529			589	47.2%	-0.08 [-0.65, 0.50]	•
Heterogeneity: Tau ² =	0.86; C	hi ² = 189	3.72, d	f = 10 (F	× ۵.۵۵۵	001); I ^z	= 95%		
Test for overall effect:	Z = 0.28	6 (P = 0.8)	30)						
Total (95% CI)			1154			1214	100.0%	-0.12 [-0.46, 0.23]	+
Heterogeneity: Tau ² =	0.63; C	hi² = 338	8.74, d	f = 22 (F	< 0.000	001); I ^z	= 94%		
Test for overall effect:	Z = 0.68	6 (P = 0.5)	51)	•					-4 -2 U 2 4
Test for subaroup diff	erences	Chi ² =	115 0	Favours (Control) Favours (Experimental)					

Fig. 5. Forest plot of store effect on GLU under 4 °C. 11 studies (2638 samples) under 4 °C measured GLU. Storage at 4 °C was much better than at RT and was stable up to 24 h.

even some enzymes LDH, AST, ALT, and ALP. The importance of normal blood potassium cannot be overemphasized and <3.5 mmol/L or >5.5 mmol/L could induce serious, even lethal arrhythmia. Nevertheless, our results showed that a sharp increase of blood potassium had occurred at the first hour under RT. Whether refrigerator storage made a difference, requires more clinical trials. Thirdly, influenced by environment factors. TBIL was a parameter increased by hemolysis and decreased by longtime exposure under sunshine, so it is not stable and changes at 3 h. under RT. DBIL was relatively stable for 24 h. as it is produced by the liver using unconjugated bilirubin. Although hemolysis leading to increased TBIL, no more DBIL was generated. BUN was another index influenced by exposure, as a result, it changed even at 3 h. under RT. ALB is an important part of plasma colloid osmotic pressure and was stable for 24 h. under RT or 4 °C and 7 d at -20 °C.

Overall, when it came to the influence of temperature, the stability appeared better when samples were stored at 4 °C compared to RT and this was much more obvious in CMP testing.

To our knowledge, this meta-analysis is the first study which systematically estimates the effect of storage conditions on CBC and CMP testing and identified that time and temperature of storage can indeed have an impact on the quality of testing. The most important implication of this study is the need to define reliable time and means of sample storage, help establish of centralized hematological services or biobanks and benefit transfusion.

Supplementary data to this article can be found online at https://doi. org/10.1016/j.ebiom.2017.09.024.

Acknowledgments

We are grateful to David R. Jobes, MD, Department of Anesthesiology and Critical Care Medicine from The Children's Hospital of Philadelphia for helpful hints in native expression.

Funding Sources

No Funding.

Conflicts of Interest

The authors declare that they have no conflict of interests.

Author Contributions

Dong-wen Wu: designed the research; searched the lecture; wrote the paper. Yu-meng Li: screened and evaluated the quality of evidence; extracted data; helped write the paper. Fen Wang: screened and evaluated the quality of evidence; extracted data.

Supplementary data Supplementary material 1 Supplementary material 2

References

- Adcock, F.D., Lippi, G., Favaloro, E.J., 2012. Quality standards for sample processing, transportation, and storage in hemostasis testing. Semin. Thromb. Hemost. 38, 576–585.
- Ashenden, M., Clarke, A., Sharpe, K., D'Onofrio, G., Plowman, J., Gore, C.J., 2013. Stability of athlete passport parameters during extended storage. Int. J. Lab. Hematol. 35, 183–192.
- Begg, C.B., Mazumdar, M., 1994. Operating characteristics of a rank correlation test for publication bias. Biometrics 50, 1088–1101.
- Briggs, C., Culp, N., Davis, B., D'Onofrio, G., Zini, G., Machin, S.J., 2014. ICSH guidelines for the evaluation of blood cell analysers including those used for differential leucocyte and reticulocyte counting. Int. J. Lab. Hematol. 36, 613–627.
- Buoro, S., Mecca, T., Seghezzi, M., Manenti, B., Cerutti, L., Dominoni, P., Napolitano, G., Resmini, S., Crippa, A., Ottomano, C., et al., 2016. Assessment of blood sample stability for complete blood count using the Sysmex XN-9000 and Mindray BC-6800 analyzers. Rev. Bras. Hematol. Hemoter. 38, 225–239.
- Daves, M., Zagler, E.M., Cemin, R., Gnech, F., Joos, A., Platzgummer, S., Lippi, G., 2015. Sample stability for complete blood cell count using the Sysmex XN haematological analyser. Blood Transfus. 13, 576–582.
- Egger, M., Davey, S.G., Schneider, M., Minder, C., 1997. Bias in meta-analysis detected by a simple, graphical test. BMJ 315, 629–634.
- Gunawardena, D., Jayaweera, S., Madhubhashini, G., Lokumarakkala, D.D., Senanayake, S.J., 2017. Reliability of parameters of complete blood count with different storage conditions. J. Clin. Lab. Anal. 31.
- Hedberg, P., Lehto, T., 2009. Aging stability of complete blood count and white blood cell differential parameters analyzed by Abbott CELL-DYN Sapphire hematology analyzer. Int. J. Lab. Hematol. 31, 87–96.
- Higgins, J.P., Thompson, S.G., Deeks, J.J., Altman, D.G., 2003. Measuring inconsistency in meta-analyses. BMJ 327, 557–560.
- Hill, V.L., Simpson, V.Z., Higgins, J.M., Hu, Z., Stevens, R.A., Metcalf, J.A., Baseler, M., 2009. Evaluation of the performance of the Sysmex XT-2000i hematology analyzer with whole bloods stored at room temperature. Lab. Med. 40, 709–718.

- Imeri, F., Herklotz, R., Risch, L., Arbetsleitner, C., Zerlauth, M., Risch, G.M., Huber, A.R., 2008. Stability of hematological analytes depends on the hematology analyser used: a stability study with Bayer Advia 120, Beckman Coulter LH 750 and Sysmex XE 2100. Clin. Chim. Acta 397, 68–71.
- Jobes, D., Wolfe, Y., O'Neill, D., Calder, J., Jones, L., Sesok-Pizzini, D., Zheng, X.L., 2011. Toward a definition of "fresh" whole blood: an in vitro characterization of coagulation properties in refrigerated whole blood for transfusion. Transfusion 51, 43–51.
- Lippi, G., Simundic, A.M., 2012. Laboratory networking and sample quality: a still relevant issue for patient safety. Clin. Chem. Lab. Med. 50, 1703–1705.
- Lippi, G., Guidi, G.C., Mattiuzzi, C., Plebani, M., 2006. Preanalytical variability: the dark side of the moon in laboratory testing. Clin. Chem. Lab. Med. 44, 358–365.
- Lombardi, G., Lanteri, P., Colombini, A., Lippi, G., Banfi, G., 2011. Stability of haematological parameters and its relevance on the athlete's biological passport model. Sports Med. 41, 1033–1042.
- Mahmoodi, M., Hajizadeh, M., Rashidinejad, H., Asadikaram, G., Khaksari, M., Mirzaee, M., Seyedi, N., Rahnema, A., Sayadi, A., 2006. Survey of changes in complete blood count and red cell indices of whole blood incubated in vitro at different temperatures up to 48 hours. J. Ayub. Med. Coll. Abbottabad 18, 14–16.
- Moher, D., Liberati, A., Tetzlaff, J., Altman, D.G., 2009. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. BMJ 339, b2535.
- Mosca, A., Paleari, R., Ivaldi, G., Galanello, R., Giordano, P.C., 2009. The role of haemoglobin A(2) testing in the diagnosis of thalassaemias and related haemoglobinopathies. J. Clin. Pathol. 62, 13–17.
- Narayanan, S., 2000. The preanalytic phase. An important component of laboratory medicine. Am. J. Clin. Pathol. 113, 429–452.
- Plebani, M., Lippi, G., 2010. Is laboratory medicine a dying profession? Blessed are those who have not seen and yet have believed. Clin. Biochem. 43, 939–941.
- Robinson, N., Sottas, P.E., Potrgiesser, T., Schumacher, Y.O., Saugy, M., 2011. Stability and robustness of blood variables in an antidoping context. Int. J. Lab. Hematol. 33, 146–153.
- Voss, S.C., Flenker, U., Majer, B., Schanzer, W., 2008. Stability tests for hematological parameters in antidoping analyses. Lab. Hematol. 14, 24–29.
- Zandecki, M., Genevieve, F., Gerard, J., Godon, A., 2007. Spurious counts and spurious results on haematology analysers: a review. Part II: white blood cells, red blood cells, haemoglobin, red cell indices and reticulocytes. Int. J. Lab. Hematol. 29, 21–41.
- Zini, G., 2014. Stability of complete blood count parameters with storage: toward defined specifications for different diagnostic applications. Int. J. Lab. Hematol. 36, 111–113.