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HAEMATOLOGY

Impact of point-of-care testing for white blood cell count on triage of patients with infection in the remote Northern Territory of Australia

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Summary

In Australia's Northern Territory (NT), acute infections are highly prevalent within Indigenous remote communities and difficulties in diagnosing the aetiology of infection are exacerbated by limited access to diagnostic tests. The objective of this study was to investigate the clinical effectiveness of point-of-care (POC) testing for total and 5-part differential white blood cell (WBC DIFF) counts for the triage of patients with possible acute infection.

The HemoCue WBC DIFF POC device was introduced into 13 remote health clinics over a 6 month period. A retrospective clinical audit of patient cases meeting the selection criteria for three acute infections (sepsis, respiratory infection and appendicitis) were examined by four registrars in duplicate; one with POC test results available and the other with POC test results removed to determine if WBC DIFF results changed or assisted in patient triage. The number of changed outcomes provided a preliminary cost-benefit analysis.

Sixty (23%) patient cases met the selection criteria for the clinical effectiveness analysis. POC test results changed the triage decision for 24 (41%) patients, of which 20 (34%) led to the prevention of an unnecessary medical retrieval and four (7%) indicated the patient had an acute infection which required a medical retrieval. POC test results assisted decision making for a further 13 (22%) patients. Cost savings related to avoiding unnecessary medical retrievals were estimated to be AU$481,440. Extrapolated NT-wide cost savings are projected to be AU$5.33 million per annum.

POC testing for WBC DIFF counts aided clinical decision making for triaging patients with three common acute infections.

Key words: White blood cell count; point-of-care testing; triage; infection; remote health.

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INTRODUCTION

Acute infections such as sepsis, appendicitis and infections within the respiratory system are highly prevalent within Indigenous members of remote communities of the Northern Territory (NT) of Australia.[1–3] A study on paediatric aerial evacuations in the Top End of the NT reported almost 50% of retrievals were due to acute infection, with respiratory infections being the most frequent (31%).[1] Another study in the Top End of the NT indicated that the hospital admissions for sepsis were amongst the highest in world at 11.8 per 1000 patients, with an even higher incidence recorded within the Indigenous population (40.8 per 1000 patients).[2] A report by the Royal Flying Doctor Service highlighted that respiratory diseases were the third most common reason for Indigenous medical retrievals after injuries and cardiovascular disease, making up around 13% of all Indigenous medical retrievals.[3]

To aid clinical decision making for these common conditions, remote health professionals often request a pathology test for a total white blood cell (WBC) and differential (DIFF) count from the laboratory. This requires a venous blood sample to be collected from the patient and sent to the nearest laboratory for analysis, with the results reported electronically to the treating doctor several days later. The transportation of blood samples to the laboratory is difficult in the remote NT due to the vast distances and climatic conditions, which can cause significant delays in the samples being received and processed by the laboratory. As WBCs are subject to degradation over time and are affected by variations in temperature, the long journey from the remote health clinic to the laboratory may cause changes in the sample integrity. A report by the International Council for Standardization in Haematology states a WBC count is only reliable if the sample is preserved with EDTA anticoagulant and stored for up to 72 hours at 4°C; beyond 72 hours and with variations in temperature the integrity of the sample may be compromised and results may be unreliable.[4] A recent study in the remote NT found that approximately 11% of WBC DIFF samples did not reach the laboratory in time for accurate measurement, with WBC results often being reported with comments indicating that results were 'unreliable' due to time delay effects or 'not reported' due to the sample not being received and processed within the designated timeframe (<72 hours).[5]

Point-of-care (POC) testing for WBC DIFF offers a potential solution to this issue as a venous or capillary blood sample can be analysed on-site during the patient consultation with results available within 5 minutes, allowing timely clinical decisions to be made.

This research study aimed to investigate clinical utility of the HemoCue WBC DIFF device for the triage of patients with three common acute medical conditions in the remote NT.

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MATERIALS AND METHODS

Ethics

Ethics approval for this study was granted by the Human Research Ethics Committee of the Northern Territory Department of Health and Menzies School of Health Research, Australia (No. 2017-2830, approved 10 April 2017).

Device selection

The HemoCue WBC DIFF (Radiometer Pacific, Australia) was selected due to its ease of use, size and ability to work off battery or AC power. The device uses imaging technology to count the total number of WBCs in a sample and provide the number and percentage of neutrophils, lymphocytes, monocytes, eosinophils and basophils as a 5-part differential within a 5 minute window. The performance of the HemoCue WBC DIFF (Radiometer Pacific, Australia) POCT device for total and 5-part differential WBC count has been previously studied in the remote NT and its operational utility has been confirmed.[5] In this previous study, the analytical quality of the WBC DIFF results was sound for all cell types except monocytes and basophils; however, in most cases, poor performance with these latter two cell types was due to the low number of cells present in the samples analysed.[5–9]

Training

Remote area nurses and medical practitioners were trained and certified as competent to perform POC testing on the WBC DIFF in this study by Flinders' scientific staff.

Site selection

Thirteen NT remote primary health care clinics with varying degrees of geographical isolation and serving differing population densities were included in the study. Three health clinics were located in the desert regions of Central Australia and ten in the tropical Top End of the NT.

Duration of study

The study period for the evaluation of the device was from April to September 2017, when the devices were on loan from Radiometer.

Clinical presentations investigated

A senior rural medical practitioner (RMP) with significant experience in remote health (RO) identified sepsis, appendicitis and respiratory infection as three common acute infectious presentations to be investigated during this study, which was of 6 months duration.

The case notes from patients who had a venous WBC DIFF POC test performed during the study period were examined to determine their suitability for inclusion in the study. To be included, the patient must have met the following criteria:

- Presented with fever (temperature >37.5°C) and one or more of the following symptoms suggestive of either sepsis (undifferentiated symptoms and no observable source), appendicitis (lower right quadrant pain and/or bowel symptoms), or respiratory infection (respiratory symptoms such as shortness of breath, sore throat, cough, sputum or abnormal chest sounds on auscultation).
- Paediatric patients and elderly patients with or without the presence of fever and with undifferentiated symptoms were also included due to the vulnerability of these patient groups to acute infection, which may present without a significant fever.

In addition, to be included in the study, the patient case notes must have included the following patient details: patient's date of birth and sex, medical history, date of presentation, details of presentation, observations (including temperature and WBC DIFF results), treatment (if applicable) and final patient outcome (i.e., whether the patient was stabilised in the remote community or was transported to a tertiary centre for further investigation or treatment by an aerial medical retrieval).

A summary of case identification is shown in the flowchart provided as Fig. 1. The inclusion and exclusion criteria were established by the study's clinical author RO.

Clinical effectiveness

To assess the clinical effectiveness of POC WBC DIFF testing, four medical registrars under the supervision of the senior RMP were chosen to review and analyse patient cases which met the inclusion criteria under the following framework. Two case scenarios were developed for each patient case for consideration by the registrars: Scenario 1 included the clinical history and presentation but excluded the WBC DIFF POC test result(s); and Scenario 2 was identical to Scenario 1 with the WBC DIFF POC test result(s) included. Neither scenario included the primary diagnosis nor the patient outcome (evacuated or remained in the community) to enable the registrars to use their own clinical judgement to decide on the impact of the WBC DIFF POC testing results.

A total of 60 cases met the selection criteria. These cases were assigned to each of the four registrars as per Table 1 to ensure a registrar did not receive Scenario 1 and 2 for the same patient case.

For Scenario 1, registrars were asked to indicate if the patient should be evacuated or remain in the community. For Scenario 2 registrars were asked to conclude if the WBC DIFF POC test result(s) 'assisted' or 'did not assist' in the clinical decision making process for the patient case.

To independently assess the quality of the registrar's decision-making, a subset of 20 patient cases (n=5 per registrar) were also reviewed by the senior RMP.

The outcomes of the registrars' deliberations on case Scenarios 1 and 2 were compared and analysed according to the flowchart in Fig. 2.

The actual patient outcome (with POC WBC DIFF test results available) was compared to the registrar's predicted patient outcome in Scenario 1 (without access to the POC WBC DIFF test results) to determine if the patient outcome 'changed' due to the availability of the on-site POC test results. If the outcomes were the same, the predicted outcomes in Scenario 1 and 2 were compared to determine if the POC WBC DIFF test results 'assisted' in the management of the patient. If the WBC DIFF results neither 'changed' nor 'assisted' in the management and/or final outcome for the patient, it was noted as 'did not assist'.

Cost benefit analysis

A preliminary cost-benefit analysis was performed to determine the potential cost savings of using the HemoCue WBC DIFF device in preventing

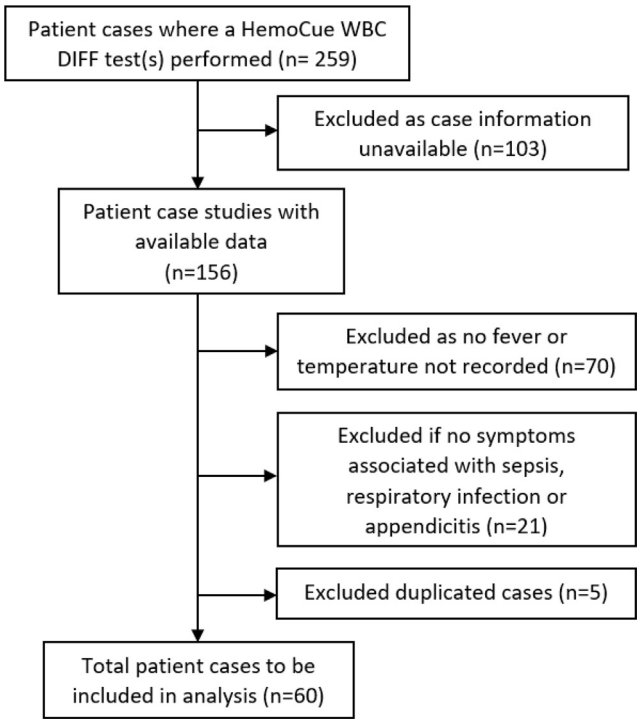

Fig. 1 Flowchart summarising reasons for case exclusion in clinical effectiveness analysis.

Table 1 Summary of patient case distribution method amongst registrars

	Registrar 1	Registrar 2	Registrar 3	Registrar 4
Subset 1 (15 cases)	Scenario 1		Scenario 2	
Subset 2 (15 cases)	Scenario 2		Scenario 1	
Subset 3 (15 cases)		Scenario 1		Scenario 2
Subset 4 (15 cases)		Scenario 2		Scenario 1
Total	30	30	30	30

unnecessary medical retrievals. A previous study has determined the average cost per medical retrieval to be AU$25,296 in the Top End to AU$17,136 in the Central Australia region of the NT.[10]

The number of patient cases determined to have a 'changed' outcome was multiplied by this average retrieval cost to provide a basic estimate of cost savings.

RESULTS

During the study period, 259 patients had a total of 442 WBC DIFF POC tests performed at the 13 health services. Complete case information was available for 156 of these patient cases. A further 96 cases were excluded for reasons identified in Fig. 1, leaving 60 cases for inclusion in the study of clinical effectiveness. The 60 patient cases comprised 33 (56%) females and 26 (44%) males with a mean age of 47 years (range 9 months–80 years). Forty-nine of the included cases came from four services, while the remaining services contributed three or less included cases. One case was removed from the final analysis as the registrars determined the case had insufficient detail to make an informed judgement.

For comparison, the excluded cases consisted of 54% females and 43% males with an average age of 40 years (range 2–76 years).

Clinical effectiveness

Analysis of the remaining 59 case scenarios by the four registrars found that access to the HemoCue WBC DIFF results 'changed' the final outcome in 24 (41%) cases and 'assisted' in management of a further 13 (22%) patients. There was 100% concordance between the registrar and RMP's assessment of outcome in the subset 20 cases assessed by both parties.

A breakdown of the patient case analysis by presentation type is provided in Fig. 3. Nine of the 59 patient cases met the selection criteria for two of the three presentation types investigated, therefore the breakdown into presentation types totaled 68 cases.

From the 24 patients where the outcome 'changed', four (17%) cases reported total WBC count >15 × 10^9 cells/L by POC, indicating the patient required a medical retrieval. In these four cases the patient would not have been evacuated if the WBC DIFF results were unavailable. In the remaining 20 (83%) cases where the outcome 'changed', normal POC WBC DIFF tests results (4–11 × 10^9 cells/L) ruled out an acute condition which enabled the patient to remain in the community, therefore preventing an unnecessary medical retrieval.

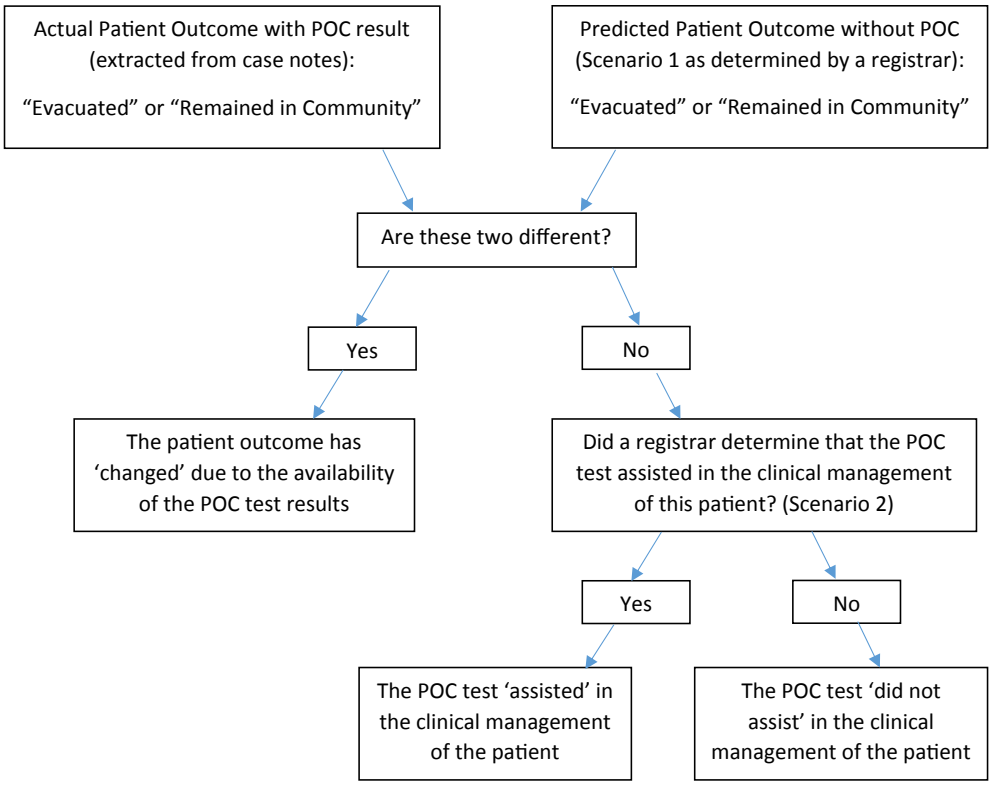

Fig. 2 Flowchart summarising the analysis of patient cases completed by the registrars.

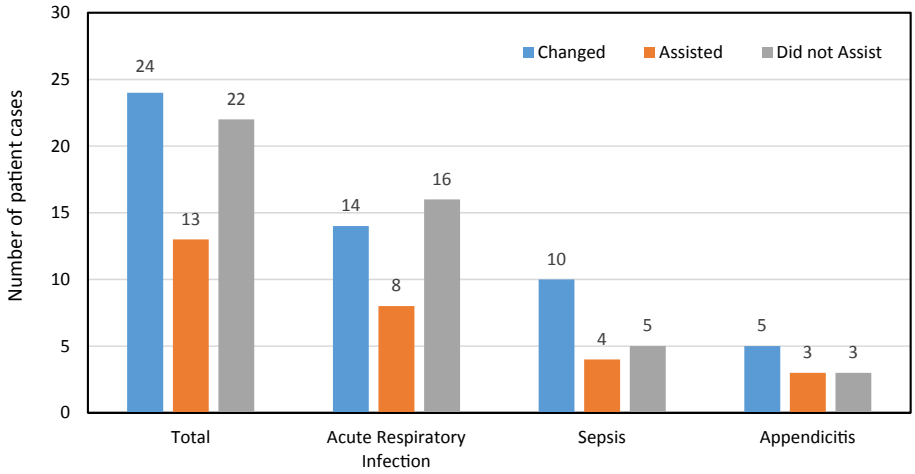

Fig. 3 Summary of patient case analysis by presentation type.

In the 13 cases where the POC test results were deemed to 'assist' in the patient's management, the WBC DIFF results provided additional evidence confirming the patient's condition and thereby assisted clinical decision making.

In the remaining 22 patient cases, the WBC DIFF results did not add any value to clinical judgement, as the decision regarding the patient's management was clear based on clinical signs and symptoms.

The following two cases, sourced as part of this study, provide real-time examples of how rapid POC WBC DIFF test results assisted in the management of patients living in remote communities.

Case study 1

Presentation

A mother presented with her 4-year-old child who had a fever and headache. The mother reported the child had not been in recent contact with any sick community members and did not have any urinary symptoms, sore throat or cough.

Examination

The child was febrile with a temperature of 39.2°C, had an increased heart rate of 160 beats per minute (reference interval 80–120) and an increased respiration rate of 40 breaths per minute (reference interval 20–30). The child was a healthy weight and had a normal haemoglobin result of 116 g/L (reference interval 102–131 g/L). A midwife examined the child and noted she had no rashes and was drinking water when offered but was listless and had some clear liquid running from her nose. Examination by the on-site RMP revealed no ear, nose or throat abnormalities, no neck stiffness and the child's chest sounds were clear.

POC test result

The HemoCue POC WBC DIFF results were normal with a total WBC count of 6.3×10^9 cells/L (reference range $4–11 \times 10^9$ cells/L).

Treatment

Based on the normal WBC results, the child was administered paracetamol and 30 minutes later her temperature had lowered to 38.8°C. However, the child now felt nauseated. The midwife considered possible viral illness or meningitis and contacted the on-call Duty RMP who requested formal blood cultures be sent to the laboratory for testing and antibiotics (ceftriaxone) to be administered. Later that evening the child become afebrile (37.6°C) and her condition improved.

Follow-up

The following morning the child was reviewed by the on-site RMP who described the child as being active and alert and requested a second POC WBC DIFF test be performed.

POC result

The HemoCue WBC DIFF results were still within the normal range with a total WBC count of 4.9×10^9 cells/L.

Summary

The RMP noted that the WBC count result assisted with the decision to keep the child in the community for monitoring and treatment as a clinically significant infection could be ruled out.

Case study 2

Presentation

A 9-year-old girl with recent knee trauma (after she dived into water and hit her right knee on a rock) presented with her right knee swollen and hot. The RMP's initial diagnosis was septic arthritis and noted that the patient's brother had a recent history of acute rheumatic fever. The patient was walking and there was no abrasion over the knee. There were also no skin lesions, except for an old dry scabies wound on her right ankle, and no history of recent tonsillitis.

Examinations

The patient was febrile (temperature 38.7°C), but had a normal heart rate, respiratory rate, blood pressure, oxygen saturation, blood glucose level and haemoglobin level, thus putting her a low risk of sepsis with a rural early warning score (REWS) of 0.[11]

POC result

The HemoCue POC WBC DIFF results were elevated with a total WBC count of 17.2×10^9 cells/L and neutrophil count of 13.6×10^9 cells/L (reference range $1.8–7.5 \times 10^9$ cells/L).

Follow-up

The on-call pediatrician advised the nurse to immediately evacuate the patient to Royal Darwin Hospital (RDH) without antibiotics unless signs of sepsis developed (such as tachycardia). However, the medical retrieval team advised they were unable to land in the remote community due to bad weather.

Treatment

Due to the delay in evacuation the pediatrician instructed the nurse to start antibiotics (flucloxacillin 50 mg/kg). Several hours later the patient was described as stable and evacuated to RDH as the weather had cleared.

Outcome

In hospital, the child was diagnosed with severe septic arthritis and osteomyelitis (infection in the bone) in her right knee, which required a long admission to hospital. On the same day the hospital laboratory total WBC count result was 17.7×10^9 cells/L and neutrophil count was 14.3×10^9 cells/L.

Summary

The treating RMP confirmed that the WBC DIFF POC test results assisted with the decision to urgently evacuate the patient as the total WBC and neutrophil count were elevated.

Cost benefit analysis

The figures from the clinical effectiveness analysis (20 prevented retrievals, 17 Top End and 3 Central Australia), and the average retrieval costs were used to provide an estimated cost saving of AU$481,440 across 6 months at the 13 health clinics. Extrapolating the cost savings to provide a NT-wide estimate over the 72 remote health clinics indicates savings upwards of AU$5 million per annum to the NT health sector (AU$5,332,874).

DISCUSSION

The POC WBC DIFF results were determined to be clinically useful in 63% of cases investigated in this study (41% where access to POC test results changed the diagnosis and 22% where the POC test result assisted the diagnosis). In general, the total WBC count was the test of most significance when deciding whether a patient retrieval was required. The case studies provide actual examples of how POC testing for WBC DIFF facilitates more patient-centred care. The first case highlighted how the WBC DIFF test assisted in preventing an expensive and culturally-stressful medical retrieval for a patient where it was unnecessary. The second case demonstrated how the WBC DIFF test increased patient safety by providing an additional tool to indicate where an evacuation may be necessary.

There are several limitations to the clinical effectiveness evaluation in this study. Firstly, one of the criteria for inclusion in the clinical effectiveness analysis was the presence of fever (temperature greater than 37.5°C), which excluded approximately one-third of patient cases where fever was absent (n=70). In these cases, the absence of fever may not have necessarily ruled out an acute condition as, for example, the patient may have self-administered paracetamol and lowered their fever prior to presentation. Secondly, the study period was from April to September during the NT's 'dry season'. The period from October to February is called the 'wet season', where extreme weather conditions including torrential rain, storms, flooding and high humidity are common and can limit the capacity of the health service to access laboratory-based pathology services. During this time, remote communities are often inaccessible by road due to flooding and aerial medical retrievals are sometimes difficult or impossible due to storms or water on the airstrips. In addition, the humid conditions are likely to increase the number of infections leading to sepsis. For these reasons, the number of patient cases where the POC testing device was used is likely to be an underestimate when considering the value of POC testing across a full year period as well as the benefit of testing with and without the presence of fever.

In addition to the acute conditions specifically investigated in this study, other niche applications of POC WBC DIFF testing were highlighted in this study through other patient case analyses. For example, four separate patients were identified where a WBC DIFF count test was performed monthly to monitor their total WBC and neutrophil count prior to having their prescription filled for clozapine, a common antipsychotic medication. The Australian guidelines recommend to only commence and continue prescribing clozapine if the total WBC count is $>3.5 \times 10^9$ cells/L and neutrophil count is $> 2.0 \times 10^9$ cells/L, as leukocytosis and neutropenia are a known side-effect of the medication.[12] Several studies have evaluated the HemoCue WBC DIFF device for monitoring clozapine and found the device to be suitable for this application.[13,14] In remote locations clozapine is often not prescribed due to the potential side effect of neutropenia, which cannot be monitored closely without the use of rapid WBC DIFF results. Another reported clinical application of the POC WBC DIFF test is to aid in the judicious prescription of antibiotics, as the overuse of antibiotics in Australia is known to be of major concern,[15] particularly in remote communities of the NT where antimicrobial resistance is high.[16] The HemoCue total WBC device (predecessor to the HemoCue WBC DIFF) has been investigated internationally for this purpose with results indicating a reduction in unnecessary antibiotic prescriptions.[17]

The preliminary cost savings associated with preventing unnecessary medical retrievals through enhancing clinical decision making are estimated to be substantial at more than AU$5 million per annum. This cost saving is also likely to significantly outweigh the cost of implementing an NT-wide POC testing network for the HemoCue WBC DIFF, which is estimated by the authors to be in the order of AU$550,000

including the cost of the device, consumables, a training and quality management program and technical support services.

Future research should include a more in-depth cost-benefit analysis of the HemoCue WBC DIFF device in assisting decision making for a broader range of clinical presentations.

CONCLUSION

POC testing for WBC DIFF counts offers an accessible, convenient and safe pathology service for patients by providing more patient-centred care. The availability of rapid WBC DIFF count results also enhances clinical decision making by remote health professionals leading to more informed triage decisions for acutely ill patients and cost savings through the prevention of unnecessary medical retrievals.

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