Background Genetic disorders are one of the leading causes of death in children admitted to neonatal and paediatric intensive care units. Genome wide sequencing (GWS), including whole genome sequencing (WGS) and whole exome sequencing (WES), uses child and parent blood samples to diagnose genetic disorders. Rapid GWS (rGWS) has a turnaround time of days to weeks allowing early diagnosis and intervention. rWES has become a standard component of early diagnostic workup and screening in critically ill children across the UK.

Objectives This review aims to evaluate the clinical utility and limitations of rGWS services in critically ill children.

Methods Literature was searched using the database Medline. Search terms included ‘Children’ and ‘rapid sequencing’. Of 96 papers, 16 primary studies were selected for comparison.

Results Studies evaluated rGWS in cohorts with median ages ranging from 7.5 days to 2.96 years. Patients were selected primarily from neonatal, paediatric or cardiac intensive care units. Diagnostic yield for rGWS, defined by the probability that the test will establish a diagnosis, ranged from 30% to 80% (mean 48%) compared to standard genetic test estimates of 10%. WGS demonstrates superiority over standard genetic tests in detection of pathogenic variants and diagnosing disorders with high genetic heterogeneity. Patients receiving the highest diagnostic yields often presented with congenital anomalies or phenotypes involving neurological, cardiovascular or renal disorders. However, the association between specific phenotypes and diagnostic yield remains controversial. Often the number of phenotypic criteria with which the child presented was positively correlated with successful diagnosis. Diagnoses may be more common in patients with a history of intrauterine growth restriction or failure to thrive.

An average of 81% of patients with successful diagnoses via rGWS subsequently received altered management, compared to 2% of those with standard genetic testing. Common management changes included avoidance of invasive investigation or treatment, targeted investigations and screening, preventative measures, sub-specialist evaluations, definitive treatment or surgery, and palliative care commencement. Genetic and reproductive counselling may constitute the majority of management changes. In those diagnosed by rGWS, 61% avoided morbidity (22% avoiding major morbidity) with no prevented morbidities in standard care cohorts. Mortality outcomes were controversial: in those diagnosed by rGWS, 61% avoided morbidity (22% avoiding major morbidity) with no prevented morbidities in standard care cohorts. Mortality ranged from 11–31% whilst 21–29% mortality was observed in undiagnosed groups.

The median turnaround time to written report was between 7.2 and 50 days (mean 16 days). However, time to blood sample analysis was more rapid and verbal reports were conveyed immediately when diagnosis would change management. rWGS was cost effective across multiple countries compared to standard genetic tests. Service challenges were primarily in optimising workflow, including efficient patient selection and sustained communication between multidisciplinary teams.

Conclusions rGWS is superior to standard genetic testing in critically ill children with regards to sensitivity, rate, diagnostic yield, management outcomes and cost effectiveness. Practical challenges can be managed with effective work flow plans and interdisciplinary communication. Future research is required to investigate the possible benefits of targeting specific phenotypes and a full UK health economics study is required to assess rGWS cost efficiency within the NHS system.