Paper Summary

<!--META_START-->

Title: AI-Driven Whole-Exome Sequencing: Advancing Variant Interpretation and Precision Medicine

Authors: Faisal Aburub, Mayyas Al-Remawi, Rami A. Abdel-Rahem, Faisal Al-Akayleh, Ahmed S.A. Ali A

DOI: 10.1109/ICCIAA65327.2025.11013653

Year: 2025

Publication Type: Conference Proceeding

Discipline/Domain: Bioinformatics / Genomic Medicine

Subdomain/Topic: Whole-Exome Sequencing, AI for Variant Interpretation, Precision Medicine

Eligibility: Eligible

Overall Relevance Score: 85

Operationalization Score: 90

Contains Definition of Actionability: Yes (implicit, as clinically actionable insights in genomic medicine)

Contains Systematic Features/Dimensions: Yes

Contains Explainability: Yes

Contains Interpretability: Yes

Contains Framework/Model: Yes (AI-driven WES pipeline with multi-omics integration and XAI)

Operationalization Present: Yes

Primary Methodology: Conceptual / Review with applied case studies

Study Context: AI-enhanced WES in clinical genetic diagnostics

Geographic/Institutional Context: University of Petra, The University of Jordan (Jordan); applied reference

Target Users/Stakeholders: Clinicians, genomic researchers, bioinformaticians, healthcare policymakers

Primary Contribution Type: Conceptual framework with practical application examples for AI-driven WES

CL: Yes

CR: Yes

FE: Yes

TI: Partial

EX: Yes

GA: Yes

Reason if Not Eligible: N/A

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AI-Driven Whole-Exome Sequencing: Advancing Variant Interpretation and Precision Medicine

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Discipline/Domain:

Bioinformatics / Genomic Medicine

Subdomain/Topic:

Whole-Exome Sequencing, AI for Variant Interpretation, Precision Medicine

Contextual Background:

The paper addresses the integration of AI—particularly ML and DL—into WES workflows to improve clini

Geographic/Institutional Context:

University of Petra (Jordan), The University of Jordan; case studies and tools from Taiwan, South Korea,

Target Users/Stakeholders:

Clinical geneticists, bioinformaticians, precision medicine practitioners, healthcare institutions.

Primary Methodology:

Conceptual framework with review of applied AI tools and comparative performance results.

Primary Contribution Type:

Framework and application roadmap for AI-driven WES in clinical precision medicine.

General Summary of the Paper

This paper presents an AI-driven framework for whole-exome sequencing (WES) that aims to improve va

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Eligibility

Eligible for inclusion: **Yes**

How Actionability is Understood

The authors implicitly define actionability as the transformation of WES data into clinically relevant, timely

> “AI… can pinpoint disease-associated variants, discover novel biomarkers, and guide personalized trea

> “Integrating multi-omics data and correlating genotype with phenotype further enable personalized inter

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What Makes Something Actionable

- Accurate identification of pathogenic variants
- Contextual relevance through phenotype-genotype correlation
- Timely reporting and reduced turnaround times
- Interpretability and transparency in AI decision-making
- Integration of multi-omics data for holistic variant assessment
- Feasibility in clinical workflows (automation, reduced manual curation)

How Actionability is Achieved / Operationalized

- **Framework/Approach Name(s):** AI-driven WES pipeline with XAI
- **Methods/Levers:** ML/DL models (DeepVariant, DANN, AI Variant Prioritizer, EVIDENCE), phenotype
- **Operational Steps / Workflow:** Data preprocessing → AI variant calling → AI-based annotation → Ph
- **Data & Measures:** WES datasets, HPO terms, population frequency databases, functional impact sc
- **Implementation Context:** Clinical genetic diagnostics and research workflows

> “An AI-powered WES pipeline… improved diagnostic yield to 41% for trio-WES cases and 28% for sing

> “Federated learning enables secure genomic data sharing… maintaining privacy and compliance” (p. 2)

Dimensions and Attributes of Actionability (Authors’ Perspective)

- **CL (Clarity):** Yes – Output must be interpretable for clinicians via XAI.
- **CR (Contextual Relevance):** Yes – Integration of patient metadata and multi-omics.
- **FE (Feasibility):** Yes – Automation and reduced turnaround time.
- **TI (Timeliness):** Partial – Reporting time reduced to one week in tested pipelines.
- **EX (Explainability):** Yes – SHAP, LIME for AI transparency.
- **GA (Goal Alignment):** Yes – Prioritization aligned with clinical diagnostic objectives.
- **Other Dimensions:** Ethical compliance, fairness, reproducibility.

Theoretical or Conceptual Foundations

- AI interpretability frameworks (SHAP, LIME)
- Federated learning privacy models

- Prior variant prioritization frameworks (ClinPred, REVEL, CADD)

Indicators or Metrics for Actionability

- Diagnostic yield percentage
- Top-N ranking accuracy for causative variants
- Turnaround time (e.g., 1 week)
- Percentage increase in pathogenic/likely pathogenic classification after AI integration

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Barriers and Enablers to Actionability

- **Barriers:** Data security, black-box AI, bias in training datasets, lack of regulatory clarity.
- **Enablers:** XAI frameworks, federated learning, inclusive datasets, standardization of AI pipelines.

Relation to Existing Literature

Positions AI-driven WES as an evolution over traditional variant interpretation pipelines, improving diagnc

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Summary

This paper conceptualizes actionability in WES as the delivery of accurate, relevant, interpretable, and tir

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Scores

- **Overall Relevance Score:** 85 — Strong implicit definition of actionability tied to AI-enhanced variant i
- **Operationalization Score:** 90 — Detailed pipeline description with tools, workflows, and metrics expli

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Supporting Quotes from the Paper

- “AI… can pinpoint disease-associated variants, discover novel biomarkers, and guide personalized treat
- “An AI-powered WES pipeline… improved diagnostic yield to 41% for trio-WES cases and 28% for singl
- “Integrating multi-omics data and correlating genotype with phenotype further enable personalized interv
- “Federated learning enables secure genomic data sharing… maintaining privacy and compliance” (p. 2)

Actionability References to Other Papers

- Huang et al. (2022) – AI Variant Prioritizer for integrating WES and phenotypic data
- Graham et al. (2018) – WES + metabolomics for variant prioritization
- Barcelona-Cabeza et al. (2021) – WES + RNA-Seq for improved variant detection

- Rusch et al. (2018) – Multi-omics integration in oncology

- Pinxten & Howard (2014) – Ethical issues in genome sequencing