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Consumer Artificial Intelligence for Pedigree Analysis: A Comparative Study in Medical Genetics

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Abstract

Background: Large language models (LLMs) are increasingly used in medical education, but their ability to analyze pedigree-based genetics problems is not well defined. This exploratory study aimed to compare the accuracy of four consumer LLMs on image-based pedigree questions and to describe the sources of their errors.

Methods: Nine pedigree cases comprising 19 sub-questions were submitted as images on May 18, 2026, to the free consumer versions of ChatGPT (GPT-5.5), Gemini (Gemini 3 Flash), Claude (Claude Sonnet 4.6), and the Microsoft Copilot app, once each in a new chat, without retries or follow-up prompts. The primary measure was accuracy, defined as the number and percentage of sub-questions answered correctly against a predefined answer key reviewed by a medical geneticist. Item-level scores were re-checked during revision using uniform rules. Incorrect answers were retrospectively classified as perception/structure, reasoning/knowledge, mixed or indeterminate errors, or as reported image-access failures.

Results: ChatGPT and Claude each answered 14 of 19 sub-questions correctly (73.7%), Copilot 11 (57.9%), and Gemini three (15.8%). Twelve of Gemini's 16 incorrect answers followed its report that it could not see or load the image. Claude's errors in the double-cousin pedigrees reflected misreading of the mating lines, whereas ChatGPT's mainly involved assigning the degree of relationship. In the single atypical pedigree (dominantly inherited hemoglobin S-Oman), no model identified the variant; Claude described dominant features but attributed them to pseudodominance because sickle cell disease is recessive.

Conclusions: In this small, single-attempt task set without statistical comparison, consumer LLMs showed variable accuracy, and errors arose both from misreading pedigrees and from misapplying genetic principles. These results do not establish a ranking of the models or an educational benefit. Consumer AI assistants should complement, not replace, formal instruction and expert supervision in medical genetics.

Categories: Genetics, Medical Education, Healthcare Technology
Keywords: artificial intelligence, chatgpt, claude, gemini, large language models, medical education, medical genetics, pedigree analysis

Introduction

Medical education is being revolutionized through AI. In theory, AI will be an integral part of medical education, serving as a collection of educational tools that provide feedback, simulate, analyze data, and develop curricula. AI is especially important in high-volume, high-stakes competency-based training environments where educators are trying to teach large amounts of content in a very short amount of time [1-3]. Several recent surveys show that this is a discipline that has transitioned from experimental to organizational in terms of adoption, especially in undergraduate and pre-clinical education, where educators are looking for ways to make learning more personalized, more digital, and more adaptable to individual needs. Scoping reviews and narrative reviews both showed that AI was heavily utilized in adaptive learning, clinical reasoning support, automated assessment, and virtual patients; similarly, both types of reviews also found that there was considerable variability across institutions and geographies regarding the use of AI in medical education [1,4-6]. The variability in the implementation of AI across institutions and geographies is critical because, by the time future physicians enter their first clinical setting, they will likely have experience using algorithmic aids for documentation, diagnosis, and decision-making. Thus, medical schools have a dual responsibility to teach students to learn using AI when it helps them learn and to teach students about AI so that students understand the potential for misuse and the limitations of AI. However, AI's application in medical education is constrained by current ethical, professional, and academic concerns. Overall, studies demonstrate that both students and educators hold favorable views of AI while expressing fears about privacy, discrimination, over-reliance, lack of transparency, cheating, and inequality in the availability of training and resources [3,4,7]. Although there are no perfect solutions to these problems, studies of chatbots have found that they have been used successfully to enhance bedside teaching and the

clinical history-taking process, but were less successful in assessing biology, image-based assessment, and critical thinking [8,9]. Large language model (LLM)-based chatbots are conversational artificial intelligence systems that have become increasingly integrated into medical education. They can explain concepts, summarize content, generate practice questions, provide rapid feedback, and support self-directed learning, making them valuable educational tools [1,2,5]. However, their effectiveness depends on appropriate task selection and academic supervision, and independent evaluation remains essential before they can be relied upon for specialized educational tasks, such as pedigree interpretation [8,9].

ChatGPT (OpenAI, San Francisco, CA) is a multimodal LLM capable of processing both text and image inputs. In this study, ChatGPT was evaluated through its free consumer interface using GPT-5.5 [10-13]. Owing to its widespread use in medical education and ability to generate explanations and educational content, ChatGPT has become one of the most commonly used AI assistants for learning [9,14]. Gemini 3 Flash (Google DeepMind, Alphabet Inc., Mountain View, CA) is a multimodal LLM capable of processing text, images, audio, video, and code [15]. During the study period, the free version was evaluated because of its wide accessibility and multimodal capabilities, which support educational tasks such as concept explanation, case analysis, and interpretation of image-based materials. According to Google, Gemini 3 Flash is designed to balance reasoning performance with speed [14,15]. Copilot (Microsoft® Corp., Redmond, WA) is a conversational AI assistant developed by Microsoft to assist with searching, writing, content generation, and information retrieval [16-18]. The consumer Copilot app evaluated in this study is distinct from Microsoft 365 Copilot, the workplace product that is integrated with applications such as Word, Excel, PowerPoint, Outlook, and Teams [16,19]; these integrations were not evaluated. Claude (Anthropic PBC, San Francisco, CA) is a multimodal family of LLMs designed for reasoning, writing, coding, and information synthesis [20]. It can process both text and images, making it suitable for educational tasks requiring multimodal interpretation [21]. The free consumer version, which used Claude Sonnet 4.6, was evaluated in this study [22]. One area in which the educational performance of LLMs remains insufficiently studied is pedigree interpretation. Pedigree analysis requires learners to integrate family history, inheritance patterns, and genetic principles and accurately interpret graphical family trees and answer associated clinical questions. Because these tasks combine visual interpretation with analytical reasoning, evaluating the performance of current LLMs in this educational context is important.

The primary objective of this study was to compare the accuracy of four consumer LLMs (ChatGPT, Gemini, Copilot, and Claude) in answering image-based pedigree interpretation questions when each question set was submitted once without follow-up prompting. Accuracy was defined as the number and percentage of sub-questions answered correctly according to a predefined answer key. The secondary objectives were to describe the main errors made by each model and to retrospectively classify incorrect answers according to whether they arose from misreading the pedigree (perception/structure errors) or from applying incorrect genetic principles or knowledge to a correctly read pedigree (reasoning/knowledge errors). No hypothesis was established before testing; the study was designed as an exploratory, descriptive comparison intended to generate rather than test hypotheses.

Materials And Methods

Study design and pedigree cases

This study compared the performance of four consumer LLMs - ChatGPT, Gemini, Copilot, and Claude - on pedigree-based medical genetics questions. A total of nine pedigree cases were included, with two to three related questions for each pedigree. The prompts and answer key contained 19 separately numbered sub-questions (two each for Pedigrees 1-6, one for Pedigree 7, and three each for Pedigrees 8 and 9), and each sub-question was scored separately. The tasks assessed inheritance pattern recognition, genotype inference, risk estimation, degree of relationship, DNA sharing, and, in one pedigree, diagnosis. The study was exploratory and descriptive, and no statistical hypothesis testing was performed.

Search strategy

A literature search was conducted using the following terms: ("large language model*" OR "generative artificial intelligence") AND ("medical genetics" OR genetic* OR inheritance OR pedigree*) AND (performance OR accuracy OR "diagnostic accuracy"), specifically targeting the title and abstract fields. Additionally, the official webpages of OpenAI (ChatGPT), Google/Google DeepMind (Gemini), Microsoft (Copilot), and Anthropic (Claude) were used to extract background information specific to each AI tool.

LLM testing procedure

All pedigrees were presented as images to preserve the visual nature of pedigree analysis. Each pedigree image and its accompanying question(s) were tested once using the official consumer version of each LLM. No retries, rewording, follow-up questions, or regenerated responses were allowed. Responses were recorded exactly as generated, and failure to interpret the pedigree image or provide a usable answer was scored as incorrect.

The exact text submitted with each pedigree image, including the answer options, is reproduced verbatim in the "Researcher Prompt" panel of the corresponding supplementary figure, alongside the unedited model

response (Appendix 1, Supplementary Figures S1-S18). The prompts consisted of the question text and answer options shown in these panels. The questions and answer options were identical across the four platforms, apart from minor formatting differences and the presence or absence of the introductory line "The following questions are related to the pedigree."

All testing was conducted on May 18, 2026. Each assistant was accessed through its free consumer interface with default settings: ChatGPT using GPT-5.5 [10-13], Gemini using Gemini 3 Flash [15], Claude using Claude Sonnet 4.6 [22], and the consumer Microsoft Copilot app [17,18], whose underlying model was not documented. Microsoft 365 Copilot and its integrations with Word, Excel, and other applications were not evaluated. Each pedigree, with its associated questions, was submitted in a new chat.

Response evaluation

Responses were compared with a predefined answer key. Performance was summarized at the pedigree level by recording the number of correctly answered sub-questions for each LLM, together with brief notes on major errors. The pedigree cases, associated questions, and answer key are provided in Appendix 2 (Supplementary Figures S19-S22).

Performance measures and scoring rules

The primary performance measure was overall accuracy, defined as the number of sub-questions answered correctly out of 19, expressed as a percentage. The secondary measures were (i) the pedigree-level score, defined as the number of correctly answered sub-questions for each pedigree; (ii) reported image-access failure, recorded when a model stated that it could not see, load, or read the pedigree image or asked the user to describe it; and (iii) the source of each error, classified as described below. The quality of explanations was described qualitatively and separately from final-answer accuracy, and correct final answers accompanied by flawed reasoning were identified.

The original protocol specified that responses were compared with the predefined answer key and that failure to interpret the pedigree image or to provide a usable answer was scored as incorrect. Detailed rules for other response types were not recorded at the time of testing. During revision, because the originally reported totals did not equal the sums of the pedigree-level scores, all item-level scores were re-checked against the recorded responses (Appendix 1, Supplementary Figures S1-S18) and the answer key (Appendix 2, Supplementary Figures S19-S22) using the following rules, applied identically to all four models. Each sub-question was scored as correct or incorrect, with no partial credit. For items with answer options, or requesting a single value or genotype, the final answer stated by the model was compared with the key, and a correct final answer was scored as correct even when the accompanying explanation was flawed. Open-ended explanation items were scored as correct only when the explanation contained the key concept specified in the answer key (genetic complementation for Pedigree 5, autosomal dominant inheritance with reduced penetrance for Pedigree 7, and the dominant sickle syndrome HbS-Oman for Pedigree 9); a partially correct explanation that omitted this concept was scored as incorrect. When a response contained internally inconsistent statements, the final answer explicitly stated was scored, and an item without an identifiable final answer was scored as incorrect. An answer given for a different individual from the one asked about was scored as incorrect. Consistent with the original protocol, when a model stated that it could not see, load, or read the pedigree image, all sub-questions for that pedigree were scored as incorrect, including answers offered from the question text alone.

This re-check changed two item scores and corrected three totals. Copilot's answer to Pedigree 1, question 1 had been scored as correct, but the recorded response selected autosomal recessive rather than X-linked recessive inheritance (Appendix 1, Supplementary Figure S10); it was rescored as incorrect. Claude’s explanation for Pedigree 9, question 3 had been scored as correct, although it attributed the pattern to pseudodominance of an autosomal recessive disorder and did not identify a dominant sickle syndrome (Appendix 2, Supplementary Figure S18); it was rescored as incorrect, consistent with the scoring of the corresponding explanations of ChatGPT and Copilot. In addition, the totals previously reported for ChatGPT (15) and Copilot (13) did not equal the sums of their pedigree-level scores (14 and 12, respectively). The corrected totals are 14 of 19 for ChatGPT, 14 for Claude, 11 for Copilot, and three for Gemini (unchanged). Because of the small number of items and the single attempt per model, results are reported descriptively, and no statistical comparisons between models were performed.

Answer-key validation

The answer key was prepared before testing and specifies the correct option or key concept for each sub-question (Appendix 2, Supplementary Figures S19-22). The predefined answer key was reviewed for accuracy by Dr Alawi Habara, a medical geneticist and coauthor of this study. Because the reviewer is a coauthor, this review was not independent, and the key was not validated by additional geneticists. For Pedigrees 3 and 4, the key defines the degree of relationship genealogically, so first cousins are third-degree relatives even when, as double first cousins, they share more DNA than ordinary first cousins.

For Pedigree 9, the key specifies sickle cell disease (SCD) as the most likely diagnosis, autosomal dominant

inheritance as the most likely mode of inheritance and, as the expected explanation, hemoglobin S-Oman (HbS-Oman), a dominant sickle syndrome in which two mutations on a single β-globin allele cause sickling in heterozygotes despite the presence of normal adult hemoglobin (HbA) (Appendix 2, Supplementary Figure S22) [23]. These answers differ in how far they can be established from the pedigree. The mode of inheritance can be inferred from the pedigree itself: affected individuals appear in each generation, affected × unaffected matings produce affected offspring of both sexes, and male-to-male transmission (I.1-II.5 and II.5-III.4) excludes X-linked inheritance. Autosomal recessive inheritance with pseudodominance cannot be excluded from the pedigree alone, but it would require all three unaffected individuals who married into the affected line (I.2, II.4, and II.7) to be carriers, which is less likely; the question therefore asked for the most likely mode of inheritance. The diagnosis of SCD rests on the clinical description in the question stem rather than on the pedigree. HbS-Oman is the expected explanation for the combination of a sickling disorder and dominant transmission, based on its published description [23], but the specific variant cannot be established from a pedigree; in a real family, hemoglobin analysis or β-globin gene testing would be required.

Retrospective error classification

Because the original scoring recorded only whether each answer was correct, each sub-question scored as incorrect was retrospectively classified during revision, using only the content of the recorded responses (Appendix 1, Supplementary Figures S1-S18). A perception/structure error was assigned when the response misidentified pedigree symbols, shading, mating lines, twin symbols, or relationships. A reasoning/knowledge error was assigned when the response described the relevant pedigree features without evident misreading but applied an incorrect genetic principle or did not apply relevant genetic knowledge. A mixed error was assigned when observable perception and reasoning mistakes both contributed. An error was classified as indeterminate when the response did not provide enough evidence to identify its source, for example, when only an answer option was given. Statements by a model that it could not see, load, or read the image were recorded separately as reported image-access failures; their technical cause could not be determined from the responses.

The classification was based only on what each response explicitly stated and does not imply knowledge of the internal processes of the models; an incorrect answer was not assumed to reflect a perception error. Correct final answers accompanied by flawed reasoning were not rescored but are identified separately. The classification was performed retrospectively without blinded or independent raters, and no agreement statistics were calculated; it is therefore descriptive and does not alter the accuracy scores.

Results

Across 19 sub-questions derived from nine pedigree cases, ChatGPT and Claude each answered 14 correctly (73.7%), Copilot answered 11 correctly (57.9%), and Gemini answered three correctly (15.8%) (Table *1*). These totals incorporate the item-level re-check described in the Materials & Methods and equal the sums of the pedigree-level scores in Table *2*. The complete AI outputs corresponding to the evaluated pedigree cases are provided in the Appendices (Supplementary Figures S1-18).

AI assistant	Total correct answers out of 19	Accuracy (%)	Most common weakness
ChatGPT	14	73.7%	Fail to handle special cases that require a deep search
Gemini	3	15.8%	Reported inability to see, load or read the pedigree image
Copilot	11	57.9%	Fail to recognize the details of a pedigree (such as a double cousin)
Claude	14	73.7%	Fail to interpret complex pedigree structures, resulting in confident but incorrect reasoning

TABLE 1: Overall scores, accuracy, and common weaknesses of ChatGPT, Gemini, Copilot, and Claude.

Pedigree	Main Concept Tested	No. of Questions	Gemini Score	Copilot Score	Claude Score	ChatGPT Score	Error Source (Retrospective)†	Key Error/Comment
1	X-linked recessive	2	0*	1	2	2	Gemini Q1-2: IA; Copilot Q1: I	ChatGPT and Claude answered both questions correctly with step-by-step genetic reasoning. Copilot gave answer-only responses and selected autosomal recessive rather than X-linked recessive inheritance, although its 100% carrier probability for II.6 was

								correct. Gemini reported that no image had been provided.
2	Mitochondrial inheritance	2	1	0*	2	2	Gemini Q1: R; Copilot Q1-2: IA	ChatGPT and Claude answered both questions correctly. Gemini read the pedigree but selected autosomal dominant inheritance; its 0% answer was correct but was reached through autosomal dominant reasoning. Copilot reported that it could not reliably read which individuals were affected.
3	DNA shared among relatives	2	0*	1	0	1	Gemini Q1-2: IA; Copilot Q1: I; Claude Q1-2: P; ChatGPT Q2: R	The pedigree shows a double first-cousin pattern (the individuals in the third generation are first cousins through both their fathers and their mothers), so they share 25% of their DNA and are third-degree relatives under the answer key. ChatGPT identified the double-cousin structure and gave 25% but classified the relationship as second degree. Copilot's answer-only response gave 12.5%, the value for ordinary first cousins, and correctly gave third degree. Claude identified the individuals as full siblings (50% DNA shared and first-degree relatives). Gemini reported that it needed to see the pedigree chart.
4	DNA shared among relatives	2	0*	1	1	0	Gemini Q1-2: IA; Copilot Q2: P; Claude Q2: P; ChatGPT Q1: P, Q2: R	The pedigree shows a double-cousin pattern from parents who are identical twins, so the individuals in the third generation share 50% of their DNA even though they are first cousins (third-degree relatives). Copilot and Claude both selected 50% but did so by reading III.1 and III.2 as full siblings, and both therefore answered first degree. ChatGPT identified the double-cousin structure but not the twin relationship of the parents and therefore answered 25%. Gemini reported that the file appeared empty.
5	Genotype interference/autosomal recessive	2	2	2	2	2	None	All four assistants explained the result by genetic complementation and gave a 100% carrier probability.
6	Autosomal dominant	2	0*	2	2	2	Gemini Q1-2: IA	ChatGPT, Claude and Copilot answered both questions correctly; in the authors' assessment, ChatGPT's explanation was easier to follow, whereas Claude's tone was more formal. Gemini reported that the image had not been uploaded or processed.
7	Autosomal dominant with penetrance	1	0*	1	1	1	Gemini Q1: IA	ChatGPT, Claude and Copilot identified autosomal dominant inheritance with reduced penetrance; Claude gave the most detailed justification. Gemini reported that the image was blank and gave general guidance only.
8	X-linked dominant	3	0	1	3	3	Gemini Q1-3: R; Copilot Q1: I, Q3: I	Copilot and Gemini selected autosomal dominant rather than X-linked dominant inheritance. For the third question, Copilot answered for II.6 rather than II.8. Gemini read the pedigree, including the affected father's affected daughters, but answered all three questions incorrectly.
9	Dominant sickle syndrome (special)	3	0*	2	1	1	Gemini Q1-3: IA; Copilot Q3: R; Claude Q2-3: R; ChatGPT Q2-3: I‡	The pedigree shows a sickle cell disease phenotype with autosomal dominant transmission, consistent with the rare dominant sickle syndrome HbS-Oman. No assistant identified HbS-Oman. Copilot identified autosomal dominant inheritance; ChatGPT and Claude selected autosomal recessive inheritance; Gemini reported that the image did not load and answered from the clinical description.
Total	All pedigrees	19	3	11	14	14	-	Totals equal the overall scores in Table 1.

TABLE 2: Pedigree-level scores, key errors, and retrospective error-source classification for each AI assistant.

* The model reported that it could not see, load, or read the pedigree image; all sub-questions for that pedigree were scored as incorrect. In Pedigree 9, Gemini's text-based answer to question 1 (sickle cell disease) matched the key but was scored as incorrect under this rule. † Retrospective classification of sub-questions scored as incorrect (see Materials & Methods; details in Table 3). ‡ Indeterminate because the pedigree image received by ChatGPT for Pedigree 9 could not be verified (Appendix 1, Supplementary Figure S5). Scores for Copilot (Pedigree 1) and Claude (Pedigree 9) reflect the item-level re-check described in the Materials & Methods. Recorded responses: ChatGPT (Supplementary Figures S1-S5); Gemini (Supplementary Figures S6-S9); Copilot (Supplementary Figures S10-S14); Claude (Supplementary Figures S15-S18; answer key (Supplementary Figures S19-S22).

P, perception/structure error; R, reasoning/knowledge error; I, indeterminate; IA, reported image-access failure; no error met the criteria for a mixed error;

Q, sub-question

Model	Pedigree, Item	Answer Given (Key)	Class	Observable Mistake (Figure)
Incorrect answers				
ChatGPT	P3 Q2	Second degree (third degree)	R	Identified III.1 and III.2 as double first cousins but assigned the degree of relationship from expected DNA sharing (25%) rather than from the genealogical relationship (2-A).
ChatGPT	P4 Q1	25% (50%)	P	Described II.1/II.2 and II.3/II.4 as ordinary sibling pairs; the twin symbols were not acknowledged, so the twin-derived 50% sharing was missed (2-B).
ChatGPT	P4 Q2	Second degree (third degree)	R	Assigned the degree of relationship from expected DNA sharing, as in Pedigree 3 (2-B).
ChatGPT	P9 Q2-3	Autosomal recessive; recessive explanation without HbS-Oman (autosomal dominant; HbS-Oman)	I‡	Stated that sickle cell disease “is inherited in an autosomal recessive pattern” and that “the pedigree perfectly matches”; the image received could not be verified (5).
Claude	P3 Q1-2	50%; first degree (25%; third degree)	P	Read III.1 and III.2 as full siblings, “both children of II.2 and II.3” (15-C).
Claude	P4 Q2	First degree (third degree)	P	Stated that the lines to II.1 and II.4 show siblings, “not additional parents”, and treated III.1 and III.2 as full siblings (16-A).
Claude	P9 Q2-3	Autosomal recessive; pseudodominance explanation (autosomal dominant; HbS-Oman)	R	Described dominant-appearing features and male-to-male transmission but attributed them to pseudodominance from assumed carrier spouses because sickle cell disease is recessive; HbS-Oman not considered (18-B).
Copilot	P1 Q1	Autosomal recessive (X-linked recessive)	I	Answer-only response; no reasoning shown (10-A).
Copilot	P2 Q1-2	No answer (mitochondrial; 0%)	IA	Stated that it could not reliably read which individuals were affected and asked the user to list them (10-B).
Copilot	P3 Q1	12.5% (25%)	I	Answer-only; the value corresponds to ordinary first cousins, but the response does not show whether the structure was misread (11-A).
Copilot	P4 Q2	First degree (third degree)	P	Stated that III.1 and III.2 “are the two children of the same parents (II.2 and II.3)” (11-B).
Copilot	P8 Q1	Autosomal dominant (X-linked dominant)	I	Answer-only response (13-B).
Copilot	P8 Q3	Second degree, for II.6 (unrelated, for II.8)	I	Answered for II.6 instead of the queried individual II.8; the source of the substitution is not evident (13-B).
Copilot	P9 Q3	Dominant explanation without HbS-Oman (HbS-Oman)	R	Identified vertical and male-to-male transmission but did not explain how a sickling disorder could be dominantly inherited (14).
Gemini	P1, P3, P4, P6, P7, P9 (12 items)	No answer or text-based answer (various)	IA	Stated that no image had been provided, that the file appeared empty or blank, that the image was not uploaded or processed, or that it did not load (6-A, 6-C, 7-A, 8-A, 8-B, 9-B).
Gemini	P2 Q1	Autosomal dominant (mitochondrial)	R	Noted affected mother I.2 with affected sons and daughters and affected fathers II.3 and II.6 with unaffected children, but did not consider exclusive maternal transmission (6-B).
Gemini	P8 Q1	Autosomal dominant (X-linked dominant)	R	Noted that affected I.1 transmitted the trait to all his daughters but chose autosomal dominant as the “simplest” explanation (9-A).
Gemini	P8 Q2	Third degree (second degree)	R	Traced III.1 to II.7 correctly but classified an aunt as a third-degree relative by counting three steps (9-A).

Gemini	P8 Q3	Third degree (unrelated)	R	Recognized II.8 as the spouse of II.7 but classified a relative by marriage ("uncle-in-law") as a third-degree relative (9-A).
Correct final answers with flawed reasoning (scored as correct)				
Copilot	P4 Q1	50% (50%)	-	Reached 50% by treating III.1 and III.2 as full siblings (11-B).
Claude	P4 Q1	50% (50%)	-	Reached 50% by treating III.1 and III.2 as full siblings (16-A).
Gemini	P2 Q2	0% (0%)	-	Reached 0% by reasoning that unaffected individuals in an autosomal dominant disorder are not carriers (6-B).

TABLE 3: Retrospective classification of incorrect answers and correct final answers reached with flawed reasoning.

Classes: P, perception/structure error; R, reasoning/knowledge error; I, indeterminate; IA, reported image-access failure. P, pedigree; Q, sub-question

Figure numbers refer to the supplementary figures of recorded responses. ‡ Indeterminate because the pedigree image received by ChatGPT for Pedigree 9 could not be verified.

ChatGPT and Claude showed similar performance across standard pedigree interpretation tasks and, in the authors' qualitative assessment, generally provided more detailed explanations than the other assistants (Table *2*). Although both chatbots obtained the same overall score, ChatGPT correctly read the double-cousin structure in Pedigree 3, whereas Claude misread the relationship in both double-cousin pedigrees (Table *2*). Copilot performed reasonably well on conventional inheritance questions but showed weakness in recognizing more complex pedigree relationships, particularly double-cousin structures. Gemini obtained the lowest score, largely because, in six of the nine pedigrees, it reported that it could not see, load, or read the image; these pedigrees were scored as incorrect under the study design. Because each model answered each question set once and no statistical testing was performed, these differences describe performance on this task set and do not establish a ranking of the models.

At the pedigree level, ChatGPT and Claude each achieved full scores in six of the nine pedigrees and obtained the highest or joint-highest score in most pedigrees. Despite the fact that both obtained the exact scores, their AI styles in answering the pedigrees differed. ChatGPT's errors were confined to the double-cousin pedigrees and the dominant sickle syndrome pedigree, whereas Claude provided extended explanations but reached incorrect conclusions in the double-cousin pedigrees because of structural misinterpretation, and in the dominant sickle syndrome pedigree. Copilot matched ChatGPT in several standard inheritance cases but lost accuracy in pedigrees requiring careful recognition of relationship structure or more detailed reasoning. All four assistants struggled with the special pedigree involving the dominant sickle syndrome scenario, and in this single case even the higher-scoring systems did not identify the atypical inheritance pattern. The screenshots of the answers for each Chatbot are in the supplementary material.

Of the 34 incorrect answers across the four models, 14 were reported image-access failures (12 for Gemini and two for Copilot), five were perception/structure errors, nine were reasoning/knowledge errors, and six were indeterminate; none met the criteria for a mixed error (Tables *2*-*3*). In six of the nine pedigrees, Gemini stated that no image had been provided, that the file appeared empty or blank, or that the image did not load (Supplementary Figures S6-S9). Its four other errors were reasoning/knowledge errors in pedigrees that it described without evident misreading; for example, in Pedigree 8 it noted that the affected father transmitted the trait to all his daughters but selected autosomal dominant inheritance (Supplementary Figure S9). Claude's errors in Pedigrees 3 and 4 were perception/structure errors, because it described III.1 and III.2 as full siblings born to II.2 and II.3 (Supplementary Figures S15-S16); its two Pedigree 9 errors were reasoning/knowledge errors. ChatGPT identified the double-cousin structure in Pedigree 3 but assigned the second degree of relationship on the basis of expected DNA sharing (a reasoning/knowledge error), and in Pedigree 4, it did not acknowledge the twin symbols (a perception/structure error) (Supplementary Figure S2). Four of Copilot's eight errors were indeterminate because its responses gave answers without explanations (Supplementary Figures S10-S14). Three correct final answers were accompanied by flawed reasoning: Copilot and Claude both selected 50% for Pedigree 4 after describing III.1 and III.2 as full siblings, and Gemini gave the correct carrier probability (0%) for Pedigree 2 after concluding autosomal dominant inheritance (Table *3*).

In the supplementary record, Supplementary Figure S5 displays the Pedigree 7 image alongside ChatGPT's response to the Pedigree 9 questions. The response refers to individuals who appear only in Pedigree 9 (II.6, II.7, and III.4-III.6), but the archived materials do not establish which image ChatGPT received. ChatGPT's Pedigree 9 answers were scored against the Pedigree 9 answer key, which does not depend on the image received, and the sources of its two errors were classified as indeterminate.

In Pedigree 9 (HbS-Oman), all four models selected SCD as the most likely diagnosis, but no response mentioned HbS-Oman, and the responses diverged on the mode of inheritance (Supplementary Figures S5, S9, S14, and S18). Claude described dominant-appearing features, stating that "at first glance the pedigree looks like it could be dominant" and noting male-to-male transmission from I.1 to II.5, and then attributed them to pseudodominance from carrier spouses, concluding autosomal recessive inheritance because SCD is "molecularly known to be an autosomal recessive hemoglobinopathy" (Supplementary Figure S18). ChatGPT concluded autosomal recessive inheritance, stating that SCD "is inherited in an autosomal recessive pattern" and that "the pedigree perfectly matches" (Supplementary Figure S5). Gemini reported that the image did not load and answered autosomal recessive on the basis of "typical presentations for this condition" (Supplementary Figure S9). Copilot identified autosomal dominant inheritance from vertical and male-to-male transmission but described the condition only as "a sickling hemoglobinopathy" without explaining how it could be dominantly inherited (Supplementary Figure S14).

Discussion

This study compares the performance of four consumer AI assistants, ChatGPT, Gemini, Claude, and Copilot, on image-based tasks involving pedigree analysis pertinent to undergraduate medical education in genetics. In this task set, ChatGPT and Claude obtained the highest accuracy; however, with 19 sub-questions, a single attempt per model, and no statistical testing, these differences are descriptive and should not be interpreted as an established ranking. Copilot showed intermediate performance, and Gemini showed poor performance, largely because it repeatedly reported that it could not see, load, or read the pedigree images. These findings demonstrate variability in the performance of consumer AI assistants on visually presented medical genetics tasks. This observation is consistent with previous studies showing that, although modern LLMs perform well on many medical knowledge tasks, visual reasoning and image interpretation remain important limitations for some models, particularly in specialized domains requiring multimodal analysis [24-26]. In the present study, this limitation was particularly evident for Gemini. One of the most important results of the current study is that the ability to succeed in a task involving pedigree-based genetics relies not only on general knowledge of medical genetics but also on proper visual perception of the pedigree structure. This was particularly so in the case of Gemini, whose low final mark followed mainly from its reported inability to see or read the pedigree images. According to the design of this study, those failures were counted as wrong because the aim was to test the real-world performance of consumer-facing tools as students would use them in real-life scenarios. The retrospective error classification is consistent with this interpretation: most of Gemini's incorrect answers followed a reported inability to see or read the image, and Claude's errors in the double-cousin pedigrees arose from misreading the pedigree lines rather than from incorrect knowledge of DNA sharing between relatives.

ChatGPT was most effective for standard pedigree questions, such as recognizing patterns of inheritance and inferring genotypes, but performed poorly on complex DNA-sharing questions. In the authors' assessment, its replies were generally comprehensive and well explained. Additionally, ChatGPT made fewer perception/structure errors than Claude in the double-cousin pedigrees, and its explanations generally set out its reasoning step by step. Such explanations may be useful to learners as a supplementary resource, but this study did not measure learning outcomes, and transparent reasoning was not always correct; for example, ChatGPT assigned double first cousins to the second degree of relationship on the basis of their expected DNA sharing. Nonetheless, good performance on the common trends must not be taken as a comprehensive reliability when it comes to rare or exceptional cases. This was manifested in one pedigree, which concerned a dominant sickle syndrome. SCD is known to be an autosomal recessive disease, but in very rare occurrences, there is an autosomal dominant type. This is the type of SCD referred to as HbS-Oman [23]. Mutations in HbS-Oman are two in a single β-globin allele, which results in super-polymerization of hemoglobin S (HbS) despite the presence of normal adult HbA [23]. The pattern could not be identified by ChatGPT, although it reached the correct diagnosis; however, in the pedigree analysis, it was diagnosed as autosomal recessive when the pedigree was clearly autosomal dominant. Moreover, it was not able to explain the scenario.

Although Claude and ChatGPT demonstrated similar accuracy levels, Claude responses were more detailed, sometimes providing information beyond the scope of the expected answer. Its main observed weakness was the misreading of complex pedigree structures. This was evident in the third pedigree, which showcased a double cousin pattern (the individuals in the third generation are first cousins from both paternal and maternal sides). In this case, Claude misinterpreted the pedigree structure entirely, identifying the individuals as full siblings (50% DNA shared and first-degree relatives) rather than double first cousins. Because Claude's responses explicitly treated III.1 and III.2 as children of the same couple, these errors were classified as perception/structure errors rather than reasoning/knowledge errors (Supplementary Figures S15-S16). This shows that, while sound and detailed knowledge of medical genetics is important, visual accuracy also plays a substantial role in correct analysis of pedigree structures.

Copilot demonstrated average performance in general and responded to a number of traditional questions on inheritance correctly; however, its weaknesses were more evident when it had to interpret accurate information with particular attention to minor details of the pedigree. This was most apparent in the two-cousin pedigrees, in which appropriate computation of shared DNA required the realization that the structure of the relationship was more complicated than that of regular first cousins. In one case, Copilot's

answer (12.5%) corresponded to the DNA sharing expected for ordinary first cousins, although its answer-only response did not show whether this reflected misreading of the pedigree or misapplication of the relationship rule. In another, it reached the correct numerical percentage only by reading III.1 and III.2 as full siblings and therefore failed to offer a biologically plausible explanation for why such a number was relevant. These results suggest that, in this task set, Copilot performed adequately on simple pedigree-related recognition tasks but was less reliable with pedigrees that have unusual or neglected architecture.

The special pedigree case of the dominant sickle syndrome scenario was the other case that all four assistants had problems with. Although this was a single case, it illustrates that even the higher-scoring systems can fail when the pedigree is characterized by a rare or unusual manifestation of genetics instead of a typical textbook picture. It suggests that success on common inheritance questions does not necessarily extend to atypical presentations, although a single pedigree cannot establish how these models perform with rare conditions in general. It also points to a potential drawback of the application of consumer AI tools to the field of genetics education without a strict approach to supervision. In outlying cases, students might be given answers that seem knowledgeable but are incomplete, simplified, or wrong.

The recorded responses to Pedigree 9 suggest a plausible explanation for this failure. SCD is conventionally taught as an autosomal recessive disorder, and in several responses, this familiar association appears to have outweighed or reshaped the dominant features shown in the pedigree. The clearest example is Claude, which acknowledged that the pedigree "looks like it could be dominant" and identified male-to-male transmission, but then reinterpreted the pattern as pseudodominance by assuming that the unaffected spouses were carriers, explicitly because SCD is "molecularly known to be an autosomal recessive hemoglobinopathy" (Supplementary Figure S18). ChatGPT likewise justified autosomal recessive inheritance by stating that SCD "is inherited in an autosomal recessive pattern" (Supplementary Figure S5); however, because the image it received cannot be verified, its response is not used here as evidence of how the Pedigree 9 image was read. Gemini, which reported that the image did not load, gave the same recessive answer from the clinical description alone (Supplementary Figure S9), showing the answer suggested by the text when no pedigree evidence is used. Conversely, Copilot read the dominant pattern correctly but did not reconcile it with the diagnosis or identify HbS-Oman (Supplementary Figure S14), indicating that a correct reading of the pedigree was not sufficient without knowledge of the rare variant. These observations are consistent with familiar textual knowledge taking precedence over pedigree evidence, but they are inferred from the outputs for a single pedigree and do not demonstrate an internal mechanism of the models. The order of the questions, in which the diagnosis was requested before the mode of inheritance, may also have encouraged anchoring on the typical inheritance of the named disease. Testing this explanation would require several atypical pedigrees, varied question order, and repeated queries.

For medical educators, this pattern has practical implications. A response that names the correct disease and gives a fluent explanation may still misrepresent the pedigree, and the error may be difficult for a novice to detect because it agrees with what the student has been taught. Educators could ask students to check an AI-generated description of a pedigree (affected individuals, matings, and transmission events) against the figure before accepting its conclusion; use atypical inheritance scenarios, such as HbS-Oman or recessive disorders showing pseudodominance, as deliberate teaching cases; and emphasize that the mode of inheritance should be inferred from the pedigree itself, with textbook associations used to check rather than replace that inference.

These findings have several possible implications for learning, although educational outcomes were not measured in this study. First, the AI assistants used by consumers may be of some use as an addition to the standard pedigree-based activities, especially when they offer well-defined step-by-step guidance. Second, their output must be taken with caution, particularly with image-based inquiries, aberrant family setups, and uncommon genetic processes. Third, wrong but plausible-sounding reasons can be especially problematic in the educational context, as they may be used to reinforce a false assumption rather than correct the misconception. The two error types also call for different safeguards: perception errors can be detected by checking that the description of the pedigree given by the AI matches the figure, whereas reasoning errors require learners to verify the genetic principle being applied. These findings suggest that AI-generated solutions should not substitute for formal instruction, answer keys, and professional guidance in medical genetics education [5,24].

This study has limitations. It was analyzed using a total of nine pedigree cases; however, there were two to three related questions per case. The sample was thus adequate in an exploratory comparative study but limited. The assistants were also given just a single attempt, with no retests, paraphrasing of statements, or additional prompts. Although this method is deliberate and is representative of a realistic consumer-use situation, it might be overly conservative in terms of predicting the performance that might be attained using iterative prompting. Nevertheless, they should not have been provided with multiple retries to test prompt optimization, but first of all, first-pass usability, which was not the objective of this study. The other limitation is that the study was narrow in that it concentrated on consumer-facing versions of the assistants, and therefore, the results cannot be considered generalizable to underlying foundation models and enterprise versions with other capabilities.

Several further limitations should be considered. No statistical testing was performed, so the differences

between models are descriptive, and learning outcomes were not measured. All testing took place on a single day using the model versions then available in the free consumer interfaces; because these models are updated frequently, the results may not be reproducible with later versions, and the underlying model of the consumer Copilot app was not documented. Detailed scoring rules for partial, contradictory, and open-ended answers were not recorded at the time of testing and were defined during revision, when the item-level re-check changed two item scores and corrected three totals. The answer key was reviewed by one medical geneticist who is also a coauthor, rather than by multiple independent geneticists; although the key for the HbS-Oman pedigree is consistent with the published description of this variant [23], independent review by several experts would strengthen confidence in the key for rare conditions. The pedigree image displayed with ChatGPT's response to Pedigree 9 (Supplementary Figure S5) does not match that response, and the image actually received could not be verified. Finally, the error-source classification was retrospective, was not performed by blinded or independent raters, had no agreement statistics, and relied on the explanations written by the models, which may not reflect how the answers were generated; answer-only responses could not be classified.

Regardless of these constraints, the study answers a practical and timely question: to what extent do frequently used consumer AI assistants solve medical genetics tasks based on pedigree when used in ways students are most likely to use them? In this task set, performance varied considerably across platforms. ChatGPT and Claude obtained the highest scores, whereas Copilot showed intermediate performance and Gemini performed poorly, largely because of its reported inability to see or read the pedigree images. Combined, these results suggest that consumer AI assistants may provide selective educational support in medical genetics, although at present their performance does not support unsupervised use in the interpretation of pedigrees.

Conclusions

In this exploratory study of nine pedigree cases, consumer LLMs showed substantial variability in their ability to solve image-based pedigree interpretation problems. ChatGPT and Claude obtained the highest scores, Copilot showed intermediate accuracy, and Gemini was markedly limited by reported failures to see or read the pedigree images; because each model was tested once and no statistical testing was performed, these differences should not be interpreted as an established ranking. Retrospective analysis of the responses indicated that errors arose both from misreading pedigree images and from misapplying genetic principles. In the single atypical pedigree tested, the familiar recessive inheritance of SCD appeared to take precedence over the pedigree evidence in some responses. Successful pedigree analysis therefore requires both accurate visual interpretation and sound genetic reasoning, and the consumer AI assistants evaluated here differed in both.

Although consumer AI assistants may serve as supplementary resources for common pedigree-based genetics problems, their educational benefit was not measured in this study, and they made errors with complex pedigree structures and with the single atypical pedigree tested. Therefore, they should complement, rather than replace, formal medical genetics teaching and expert supervision. Continued evaluation of these rapidly evolving models, including repeated testing, larger and more varied pedigree sets, and studies of learning outcomes, will be essential to define their appropriate role in genetics education.

Appendices

Appendix 1

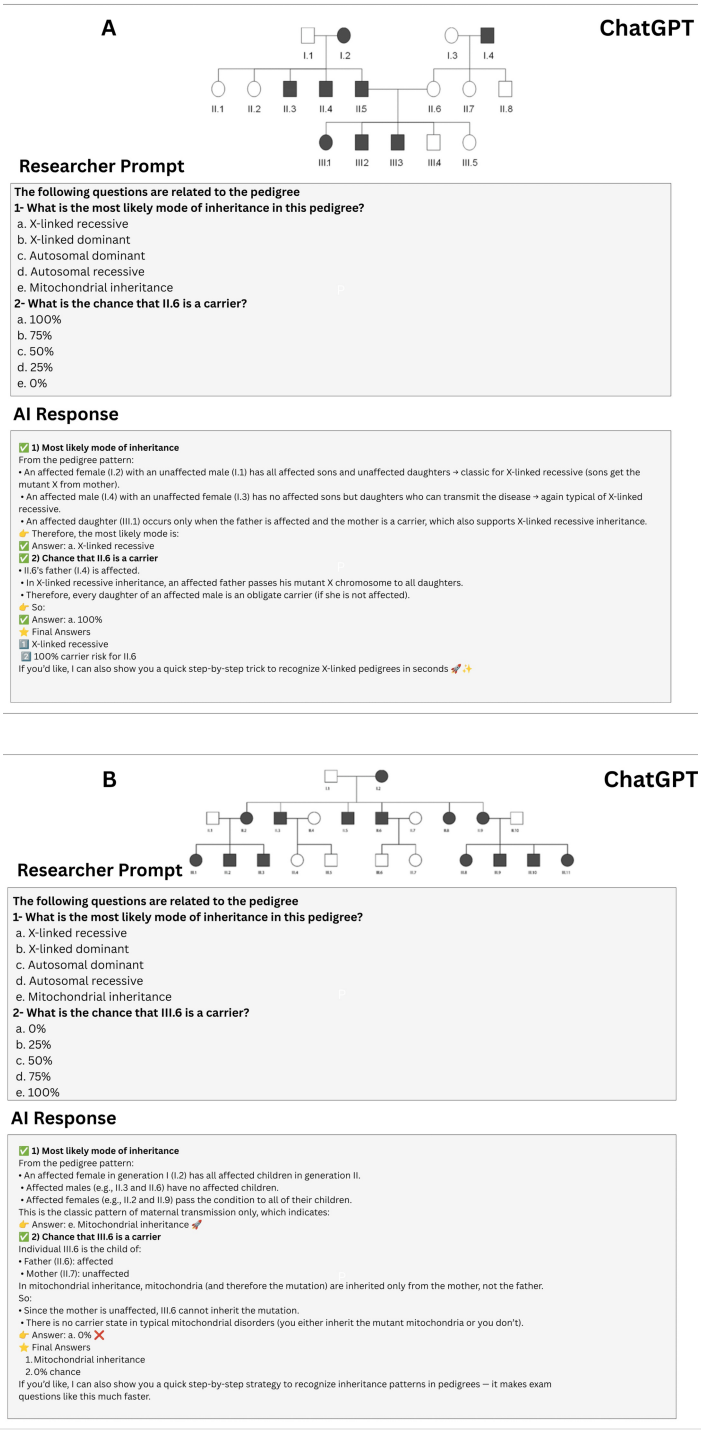
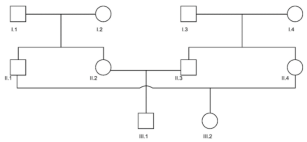


FIGURE 1: Panel A shows ChatGPT's response to Pedigree 1, and Panel B shows ChatGPT's response to Pedigree 2.

A **ChatGPT**



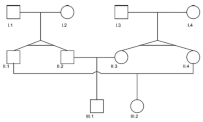
Researcher Prompt

The following questions are related to the pedigree
1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
a. 12.5%
b. 25%
c. 37.5%
d. 50%
e. 62.5%
2- What is the degree of relative between III.1 and III.2
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated

AI Response

From the pedigree:
• I.1 & I.2 are parents of II.1 and II.2
• I.3 & I.4 are parents of II.3 and II.4
Then:
• II.2 marries II.3 → child = III.1
• II.1 marries II.4 → child = III.2
So III.1 and III.2 share both sets of grandparents (I.1–I.2 and I.3–I.4). This makes them double first cousins 👫
✅ **1) Average amount of DNA shared**
• First cousins normally share 12.5%
• Double first cousins share twice that = 25%
⭐ Therefore the correct answer is: → b. 25%
✅ **2) Degree of relationship**
Relatives who share about 25% DNA are classified as:
• Parent–child
• Full siblings
• Double first cousins
These are considered 2nd-degree relatives 🧬
⭐ Therefore the correct answer is: → b. 2nd degree
✅ Final Answers
1️⃣ 25%
2️⃣ 2nd degree
If you want, I can also show you a quick trick to calculate DNA sharing in pedigrees step-by-step — it makes these questions very easy 👍

B **ChatGPT**



Researcher Prompt

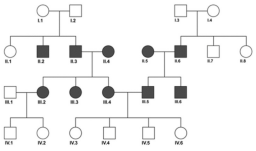
The following questions are related to the pedigree
1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
a. 12.5%
b. 25%
c. 37.5%
d. 50%
e. 62.5%
2- What is the degree of relative between III.1 and III.2
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated

AI Response

From the pedigree:
• II.1 and II.2 are siblings (children of I.1 & I.2).
• II.3 and II.4 are siblings (children of I.3 & I.4).
Then:
• II.2 × II.3 → child = III.1
• II.1 × II.4 → child = III.2
So III.1 and III.2 are "double first cousins" 👫 They are related through both parents' sides (their fathers are brothers and their mothers are sisters).
✅ **1) Average amount of DNA shared**
• First cousins normally share 12.5% (1/8) 🧬
• But double first cousins share twice that because they are related through two independent sibling pairs.
1/8 + 1/8 = 1/4 = 25%
⭐ Correct answer: b. 25%
✅ **2) Degree of relationship**
Relationship degrees are based on expected DNA sharing:
• 1st-degree: 50% (parent–child, full siblings)
• 2nd-degree: 25% (grandparent–grandchild, half-siblings, double first cousins)
• 3rd-degree: 12.5% (first cousins)
Since III.1 and III.2 share ~25%, they are:
⭐ Correct answer: b. 2nd degree
✅ Final Answers:
1. 25%
2. 2nd-degree relatives
If you'd like, I can also show you a quick shortcut method to calculate DNA sharing in pedigrees like this — it makes exams much faster ⚡🙂

FIGURE 2: Panel A shows ChatGPT's response to Pedigree 3, and Panel B shows ChatGPT's response to Pedigree 4.

A **ChatGPT**



Researcher Prompt

1- This pedigree is for a non-syndromic (congenital) deafness in humans that is inherited usually as an autosomal recessive condition. In the following pedigree, two deaf individuals, III.4 and III.5, have married and given birth to four children with normal hearing. Propose an explanation.

2- What are the chances for individuals IV.3, IV.4, IV.5, and IV.6 to be carriers?

AI Response

✅ **1) Explanation for why two deaf parents have normal-hearing children**
Although non-syndromic congenital deafness is usually autosomal recessive, it is also genetically heterogeneous (a key concept in Genetics). 👉 This means mutations in different genes can cause the same phenotype (deafness).
In this pedigree:
• Individual III.4 may be deaf because she is homozygous recessive at gene A → genotype: aaBB
• Individual III.5 may be deaf because he is homozygous recessive at a different gene B → genotype: AAbb
When they marry: aaBB × AAbb → all children AaBb
✨ Each child receives:
• a normal allele A from the father
• a normal allele B from the mother
So all children have at least one functional copy of BOTH genes → normal hearing.
This phenomenon is called: ✅ Genetic complementation (locus heterogeneity)
Both parents are deaf, but for different genetic reasons, so their mutations "complement" each other.
✅ **2) Chance that IV.3, IV.4, IV.5 and IV.6 are carriers**
From the cross: aaBB × AAbb
All offspring must be: AaBb
Therefore: 👉 Each child is an obligate carrier at BOTH loci.
So the probability that any of the following individuals is a carrier:
• IV.3
• IV.4
• IV.5
• IV.6
👉 Carrier probability = 100% (certain).
They are:
• phenotypically normal (hearing)
• but heterozygous for mutations in two different deafness genes

B **ChatGPT**



Researcher Prompt

1- What is the most likely mode of inheritance in this pedigree?
a. X-linked recessive
b. X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
2- What is the most likely genotype of individual I.1 for the disease-causing mutation?

AI Response

✅ **1) Most likely mode of inheritance**
The pedigree shows:
• Affected individuals in every generation (vertical transmission)
• Both males and females affected
• Father-to-son transmission present (I.1 → II.6 / II.7)
Father-to-son transmission rules out X-linked inheritance ❌
Equal sex distribution rules out mitochondrial ❌
Unaffected parents do not produce affected children consistently (so not typical autosomal recessive) ❌
👉 Therefore, the most likely mode of inheritance is:
✅ c. Autosomal dominant
✅ **2) Most likely genotype of individual I.1**
Individual I.1 is affected, but he has both affected and unaffected children with an unaffected partner.
If the disorder is autosomal dominant, then:
• A homozygous dominant (AA) parent would pass the disease to all children
• Since some children are unaffected, I.1 cannot be AA
👉 Therefore, the most likely genotype is:
✅ Heterozygous (Aa)
⭐ Final Answers
1.c. Autosomal dominant
2.I.1 genotype: Heterozygous (Aa)

FIGURE 3: Panel A shows ChatGPT's response to Pedigree 5, and Panel B shows ChatGPT's response to Pedigree 6.

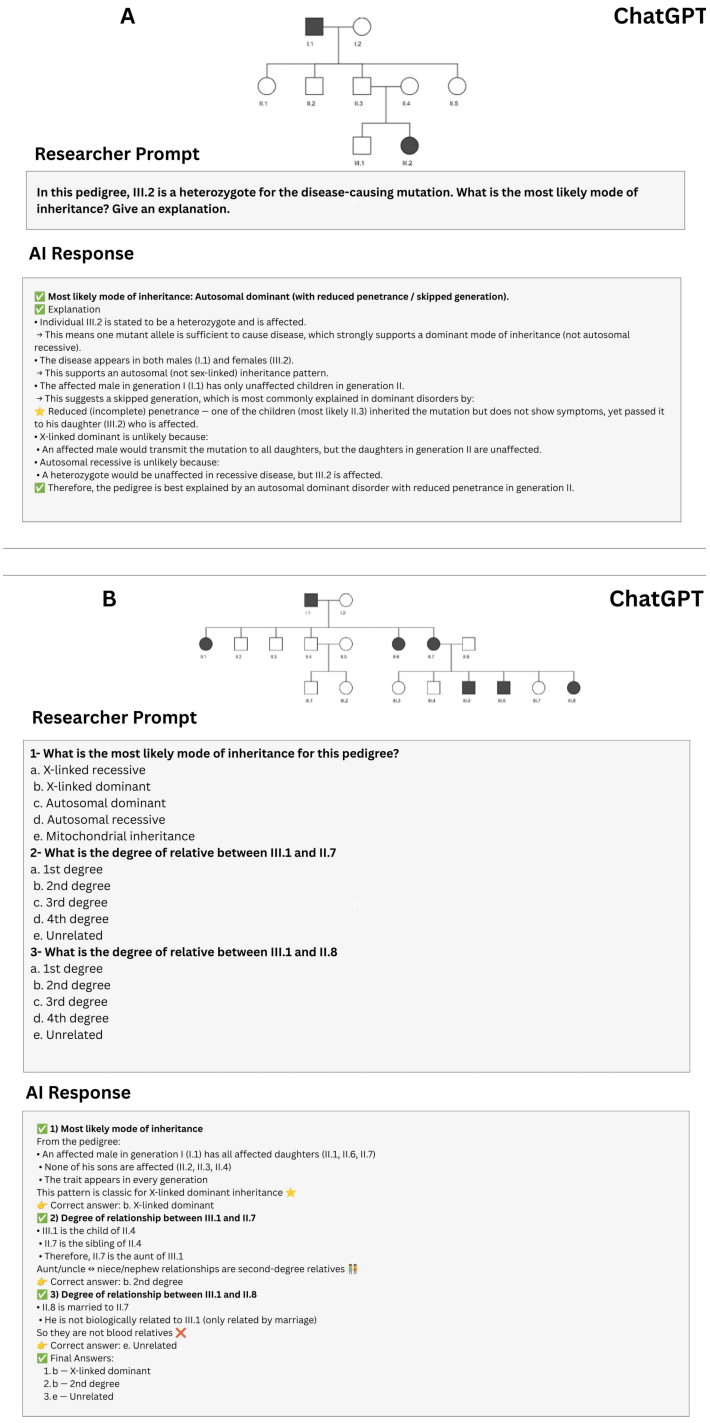
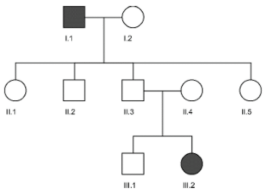


FIGURE 4: Panel A shows ChatGPT's response to Pedigree 7, and Panel B shows ChatGPT's response to Pedigree 8.

ChatGPT



Researcher Prompt

The following pedigree is for a family affected by an inherited blood disorder characterized by hemolytic anemia and recurrent painful episodes
1- What is the most likely disease
a. Sickle cell disease
b. G6PD deficiency
c. β-thalassemia
d. α-thalassemia
2- What is the likely mode of inheritance in this pedigree
a. X-linked recessive
b. X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
3- Based on this pedigree, explain how the mode of inheritance supports the most likely disease diagnosis.

AI Response

✅ **1) Most likely disease**
The description (hemolytic anemia + recurrent painful episodes) together with the pedigree strongly suggests:
👉 Answer: a. Sickle cell disease
Why?
• Painful vaso-occlusive crises are classic and very characteristic of sickle cell disease 🩸
• Thalassemia mainly causes anemia and bone changes, but recurrent painful crises are not typical
• G6PD deficiency causes episodic hemolysis after triggers (drugs, fava beans, infection), not chronic painful crises
✅ **2) Likely mode of inheritance**
👉 Answer: d. Autosomal recessive
✅ **3) How the pedigree supports this diagnosis**
Let's interpret the pedigree step-by-step 🧬:
⭐ Key pedigree features
1. Affected individuals are born to unaffected parents
• Example: Generation II shows unaffected couples having affected children (III.4, III.5, III.6).
• This is a hallmark of autosomal recessive inheritance.
1. Both males and females are affected
• Rules out X-linked recessive (which affects mostly males).
• Also rules out X-linked dominant patterns.
1. Disease can skip generations
• Seen in recessive traits when carriers are phenotypically normal.
1. Affected × unaffected mating produces ~50% affected offspring
• Seen in II.6 (affected) × II.7 (carrier/unaffected) → one affected and one unaffected child.
• This matches aa × Aa → 50% aa (affected).
⭐ Why this supports sickle cell disease specifically
• Sickle cell disease is inherited in an autosomal recessive pattern
• The pedigree perfectly matches:
• Carrier parents → affected child
• Equal sex distribution
• Generation skipping
• matches inheritance pattern of sickle cell disease
Combined with the clinical clue (painful hemolytic crises) → makes sickle cell disease the most likely diagnosis 👌
✅ Final Answer Summary
1️⃣ Most likely disease → Sickle cell disease
2️⃣ Mode of inheritance → Autosomal recessive
3️⃣ Pedigree supports diagnosis because:
• unaffected parents produce affected children
• both sexes affected
• disease skips generations
• matches inheritance pattern of sickle cell disease

FIGURE 5: ChatGPTs response to Pedigree 9.

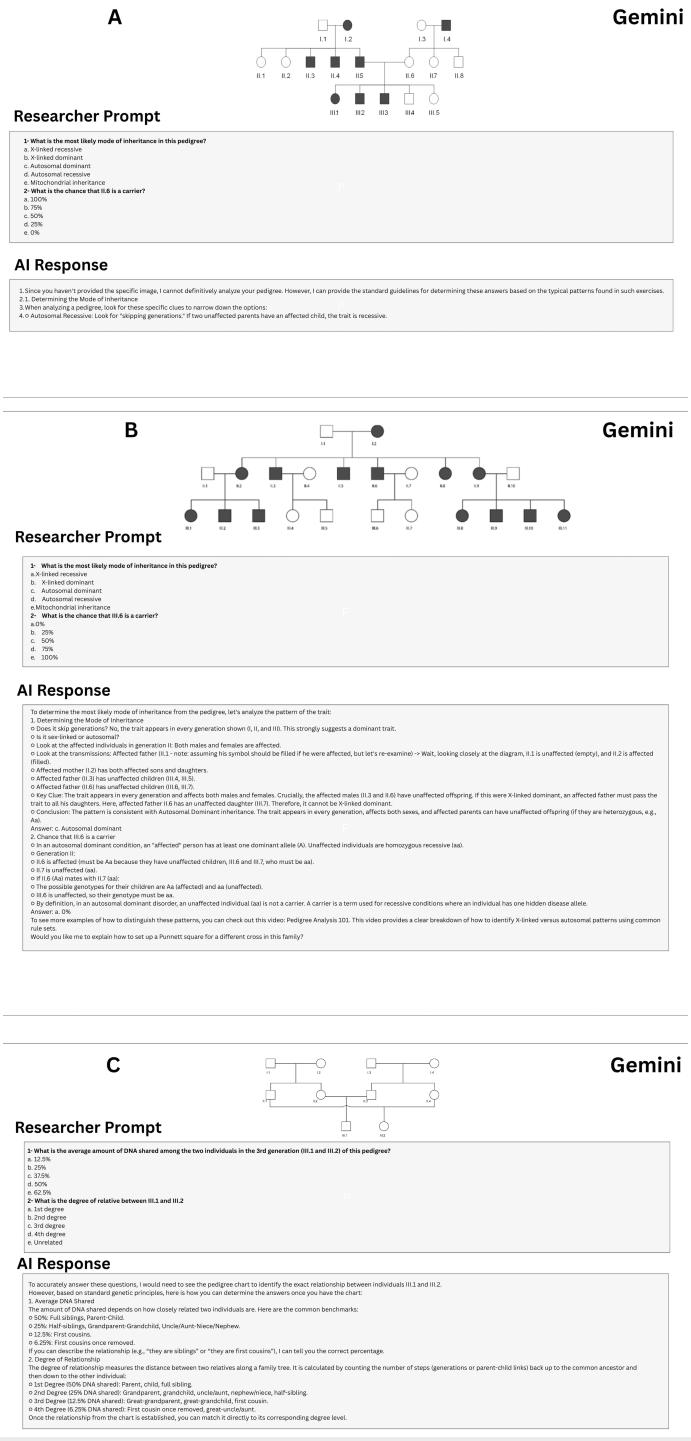
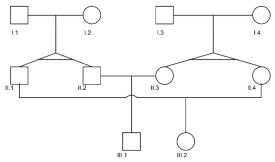


FIGURE 6: Panel A shows Gemini's response to Pedigree 1, Panel B shows Gemini's response to Pedigree 2, and Panel C shows Gemini's response to Pedigree 3.

A **Gemini**



Researcher Prompt

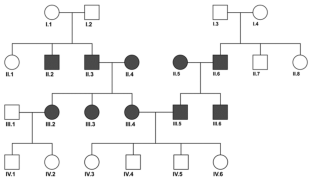
1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
a. 12.5%
b. 25%
c. 37.5%
d. 50%
e. 62.5%
2- What is the degree of relative between III.1 and III.2
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated

AI Response

To determine the answers, we need to analyze the pedigree chart (which you provided as Picture4.png). Although the file content appears empty in this system, I can guide you through the logic needed to solve these problems based on standard pedigree analysis.
Determining Relationship and DNA Sharing
To find the average amount of DNA shared and the degree of relationship, follow these steps using the pedigree:

1. Identify the Path: Trace the path from individual III.1 back to the most recent common ancestor(s) shared with individual III.2, and then down to III.2.
   - Calculate the Coefficient of Relationship (r):The formula for the coefficient of relationship between two individuals is $r = \sum(1/2)^n$, where n is the number of steps in the path connecting the two individuals through their common ancestor(s).
     - Common relationships:Parent/Child: n = 1, $r = (1/2)^1 = 0.5$ (50%).
     - Full Siblings: n = 2, r = 1/2 (50%).

B **Gemini**



Researcher Prompt

1. **This pedigree is for a non-syndromic (congenital) deafness in humans that is inherited usually as an autosomal recessive condition. In the following pedigree, two deaf individuals, III.4 and III.5, have married and given birth to four children with normal hearing. Propose an explanation.**

2. **What are the chances for individuals IV.3, IV.4, IV.5, and IV.6 to be carriers?**

AI Response

It sounds like you are analyzing a classic scenario in genetics regarding genetic heterogeneity. Even though the pedigree indicates a condition (non-syndromic deafness) that is typically autosomal recessive, the fact that two affected parents can have children with normal hearing provides a key insight.
1. Explanation: Genetic Heterogeneity (Complementation)
The most plausible explanation is that the two parents (III.4 and III.5) are homozygous for mutations in different genes that both cause deafness.

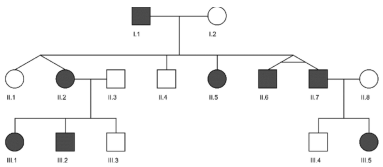
- Autosomal Recessive Inheritance: In this mode, an individual needs two non-functioning copies (alleles) of a specific gene to manifest the condition. Let's denote the two different genes as Gene A and Gene B.
  - The Scenario:Parent III.4 could have a genotype of aaBB (homozygous recessive for Gene A, but wild-type for Gene B).
  - Parent III.5 could have a genotype of AAbb (wild-type for Gene A, but homozygous recessive for Gene B).
- The Outcome: When they have children, each child inherits one allele from each parent for both genes. Every child would then have the genotype AaBb. Because they have at least one functional, dominant copy of both Gene A and Gene B, they will all have normal hearing.

This phenomenon is known as genetic complementation: the wild-type allele from one parent "complements" the mutant allele from the other, restoring the normal phenotype.
2. Chances for Individuals IV.3, IV.4, IV.5, and IV.6 to be Carriers
In the scenario described above (aaBB × AAbb → AaBb), all of the children (the F1 generation, or in your pedigree, individuals IV.3 through IV.6) are obligate double heterozygotes.

- Because they possess one copy of the recessive allele for Gene A (a) and one copy of the recessive allele for Gene B (b), they are technically carriers for both forms of deafness.
- Therefore, the probability that any of these children is a carrier for Gene A is 100%, and the probability that any of them is a carrier for Gene B is 100%.

FIGURE 7: Panel A shows Gemini's response to Pedigree 4, and Panel B shows Gemini's response to Pedigree 5.

A **Gemini**



Researcher Prompt

1 - What is the most likely mode of inheritance in this pedigree?
a.X-linked recessive
b. X-linked dominant
c.Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance

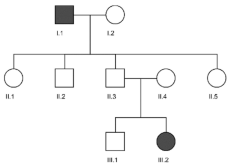
2- What is the most likely genotype of individual I.1 for the disease-causing mutation?

AI Response

It appears that the image of the pedigree was not correctly uploaded or processed, as the file content returned as empty. To provide an accurate analysis, I need to be able to see the specific patterns in the pedigree (such as which generations are affected, the sex of the affected individuals, and whether the trait skips generations).
However, I can provide you with the general guidelines to determine the mode of inheritance and the genotype of individual I.1 once you have the image in front of you.
1. Determining the Mode of Inheritance
When analyzing a pedigree, look for these key patterns:

- Autosomal Dominant: The trait appears in every generation. Every affected individual has at least one affected parent. Both males and females are affected with roughly equal frequency.
- Autosomal Recessive: The trait often skips generations. Affected individuals can have unaffected parents (both parents must be carriers). Both males and females are affected with roughly equal frequency.
- X-Linked Dominant: Similar to autosomal dominant, it appears in every generation. However, an affected father will pass the trait to all of his daughters but none of his sons.

B **Gemini**



Researcher Prompt

In this pedigree, III.2 is a heterozygote for the disease-causing mutation. What is the most likely mode of inheritance? Give an explanation.

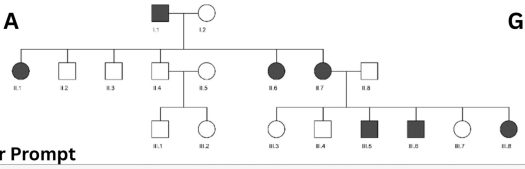
AI Response

To determine the most likely mode of inheritance in a pedigree when an individual (III.2) is identified as a heterozygote for a disease-causing mutation, we must look at how the trait is expressed in the family tree.
Because I cannot see the specific family relationships in your file (the image was blank), I will guide you through the logic used to analyze such a pedigree based on your finding that III.2 is a heterozygote.
1. The Core Logic: Is the Trait Dominant or Recessive?

- If the trait is Autosomal Recessive: Individuals who are heterozygous (Aa) are unaffected carriers. They do not show the disease phenotype. If III.2 is a carrier, this is consistent with an autosomal recessive pattern, provided the disease only appears in individuals who are homozygous recessive (aa).
  - Look at the pedigree: Do you see affected individuals (shaded) born to two unaffected parents? If so, this strongly supports autosomal recessive inheritance.
- If the trait is Autosomal Dominant:
- An individual who is heterozygous (Aa) would be affected by the disease, because only one copy of the mutation is needed to express the trait. If III.2 is a heterozygote and is affected, this fits autosomal dominant inheritance.
  - Look at the pedigree: Is the disease present in every generation, with every affected person having at least one affected parent? If so, this points to autosomal dominant inheritance.

FIGURE 8: Panel A shows Gemini's response to Pedigree 6, and Panel B shows Gemini's response to Pedigree 7.

A **Gemini**



Researcher Prompt

1- What is the most likely mode of inheritance for this pedigree?
a. X-linked recessive
b.X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
2-What is the degree of relative between III.1 and II.7
a.1st degree
b. 2nd degree
c.3rd degree
d.4th degree
e.Unrelated
3-What is the degree of relative between III.1 and II.8
a.1st degree
b.2nd degree
c.3rd degree
d.4th degree
e. Unrelated

AI Response

Based on the provided pedigree, here is the analysis for your questions:
1. Most Likely Mode of Inheritance
The most likely mode of inheritance is c. Autosomal dominant.
Reasoning:
- Presence in every generation: The trait appears in generation I, II, and III.
- No male-to-male transmission skip: An affected father (I.1) transmits the trait to his daughters (II.1, II.6, II.7).
- Affected offspring have an affected parent: Every affected individual has at least one affected parent.
- No sex bias: Both males and females are affected, which is typical for autosomal traits. While X-linked dominant is theoretically possible, autosomal dominant is generally the "simplest" explanation when no definitive evidence (like affected fathers having unaffected daughters) contradicts it.

2. Degree of Relationship between III.1 and II.7
The relationship between III.1 and II.7 is c. 3rd degree.
Reasoning:
Degrees of relationship are calculated by counting the steps (meioses) between two individuals:
1. III.1 to II.4 (parent/child) = 1 step.
2. II.4 to I.1 (child/parent) = 1 step.
3. I.1 to II.7 (parent/child) = 1 step.
4. Total = 3 steps (3rd degree). They are effectively an uncle/aunt and nephew relationship.

3. Degree of Relationship between III.1 and II.8
The relationship between III.1 and II.8 is c. 3rd degree.
Reasoning:
1. III.1 to II.4 (child/parent) = 1 step.
2. II.4 to I.1 (child/parent) = 1 step.
3. I.1 to II.7 (parent/child) = 1 step.
4. II.7 to II.8 (spouses) — This connection is through marriage. However, in pedigree degree calculations, you trace the bloodline. Since II.8 is the spouse of II.7, and II.7 is an aunt to III.1, II.8 is an uncle-in-law.

B **Gemini**



Researcher Prompt

The following pedigree is for a family affected by an inherited blood disorder characterized by hemolytic anemia and recurrent painful episodes
1-What is the most likely disease
a.Sickle cell disease
b.G6PD deficiency
c.β-thalassemia
d.α-thalassemia
2-What is the likely mode of inheritance in this pedigree
a. X-linked recessive
b. X-linked dominant
c.Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
3- Based on this pedigree, explain how the mode of inheritance supports the most likely disease diagnosis.

AI Response

Based on the clinical presentation described, here are the answers to your questions. Please note that because the image file provided did not load, I am basing the inheritance pattern analysis on typical presentations for this condition.
1. Most Likely Disease
The correct answer is a. Sickle cell disease.
- Rationale: Sickle cell disease is characterized by chronic hemolytic anemia and recurrent, painful vaso-occlusive episodes (often called "pain crises"). While G6PD deficiency and thalassemias are also inherited hemolytic anemias, they do not classically present with the characteristic, severe, recurrent painful crises that are the clinical hallmark of sickle cell disease.

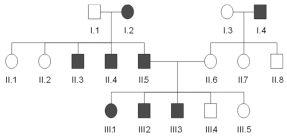
2. Likely Mode of Inheritance
The correct answer is d. Autosomal recessive.
- Rationale: Sickle cell disease is an autosomal recessive disorder. This means that for an individual to be affected, they must inherit two copies of the abnormal hemoglobin S gene (one from each parent).

3. Explanation of Inheritance Pattern
In a pedigree chart, an autosomal recessive condition typically shows the following patterns, which support the diagnosis of sickle cell disease:
- "Skipping" Generations: Affected individuals often appear in generations where neither parent is affected. This indicates that both parents are asymptomatic "carriers" (heterozygous, carrying one normal allele and one disease allele).
- Equal Prevalence: Both males and females are affected with equal frequency because the gene is located on an autosome (a non-sex chromosome), not on the X or Y chromosome.
- Consanguinity: In some pedigrees, you may see marriages between close relatives (consanguinity), which increases the mathematical probability that both parents carry the same rare recessive mutation.

Next Step: Would you like me to explain the specific genetic mechanism (the mutation in the β-globin gene) that causes the red blood cells to sickle?

FIGURE 9: Panel A shows Gemini's response to Pedigree 8, and Panel B shows Gemini's response to Pedigree 9.

A **Copilot**



Researcher Prompt

1- What is the most likely mode of inheritance in this pedigree?
a. X-linked recessive
b. X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
2- What is the chance that II.6 is a carrier?
a. 100%
b. 75%
c. 50%
d. 25%
e. 0%

AI Response

1. Most likely mode of inheritance:
d. Autosomal recessive
1. Chance that II.6 is a carrier:
a. 100%

B **Copilot**



Researcher Prompt

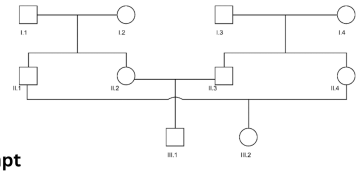
1- What is the most likely mode of inheritance in this pedigree?
a.X-linked recessive
b. X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e.Mitochondrial inheritance
2- What is the chance that III.6 is a carrier?
a.0%
b. 25%
c. 50%
d. 75%
e. 100%

AI Response

I can't reliably read which specific individuals are affected from the diagram alone, and that detail is crucial here.
To work this out properly, I need you to tell me:
• Exactly which individuals are shaded (affected) — for example: I.1, II.3, II.7, III.2, etc.
Once you list the affected individuals, I can:
1. Identify the most likely mode of inheritance from the options.
2. Calculate the chance that III.6 is a carrier and pick the correct percentage.

FIGURE 10: Panel A shows Copilot's response to Pedigree 1, and Panel B shows Copilot's response to Pedigree 2.

A **Copilot**



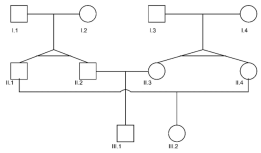
Researcher Prompt

1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
a. 12.5%
b. 25%
c. 37.5%
d. 50%
e. 62.5%
2- What is the degree of relative between III.1 and III.2
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated

AI Response

Average DNA shared between III.1 and III.2:
-> a. 12.5%
Degree of relationship between III.1 and III.2:
-> c. 3rd degree

B **Copilot**



Researcher Prompt

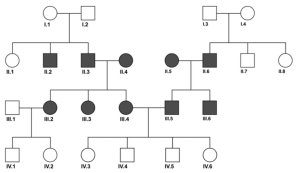
1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
a. 12.5%
b. 25%
c. 37.5%
d. 50%
e. 62.5%
2- What is the degree of relative between III.1 and III.2
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated

AI Response

Good question, and nice clear pedigree.
Average DNA shared between III.1 and III.2:
III.1 and III.2 are siblings, since they are the two children of the same parents (II.2 and II.3). Full siblings share an average of 50% of their DNA.
✅ Answer: d. 50%
Degree of relationship between III.1 and III.2:
Full siblings are first-degree relatives.
✅ Answer: a. 1st degree

FIGURE 11: Panel A shows Copilot's response to Pedigree 3, and Panel B shows Copilot's response to Pedigree 4.

A **Copilot**



Researcher Prompt

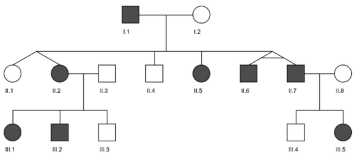
1. **This pedigree is for a non-syndromic (congenital) deafness in humans that is inherited usually as an autosomal recessive condition. In the following pedigree, two deaf individuals, III.4 and III.5, have married and given birth to four children with normal hearing. Propose an explanation.**

2. **What are the chances for individuals IV.3, IV.4, IV.5, and IV.6 to be carriers?**

AI Response

- The best explanation is locus (gene) heterogeneity with complementation.
- ◦ III.4 is homozygous recessive for a mutation at one deafness gene (e.g. aaBB),
- ◦ III.5 is homozygous recessive for a different deafness gene (e.g. AAbb).
- Each child receives one normal allele at each locus (AaBb), so all four are phenotypically normal despite both parents being deaf.
- Under this model, each of IV.3, IV.4, IV.5, and IV.6 must be carriers for both mutant genes (genotype AaBb).
- ◦ So the chance for each of them to be a carrier is 100%.

B **Copilot**



Researcher Prompt

1 - What is the most likely mode of inheritance in this pedigree?
a.X-linked recessive
b. X-linked dominant
c.Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance

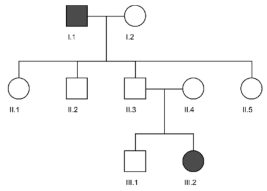
2- What is the most likely genotype of individual I.1 for the disease-causing mutation?

AI Response

Most likely mode of inheritance:
c. Autosomal dominant
◦ Affected males and females
◦ Male-to-male transmission
◦ Trait appears in every generation
Most likely genotype of individual I.1:
Heterozygous for the mutation (Aa)
◦ Because he is affected, but has both affected and unaffected children with an unaffected partner, which fits an autosomal dominant heterozygote.

FIGURE 12: Panel A shows Copilot's response to Pedigree 5, and Panel B shows Copilot's response to Pedigree 6.

A **Copilot**



Researcher Prompt

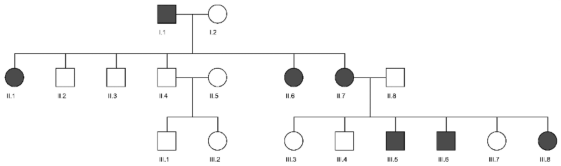
In this pedigree, III.2 is a heterozygote for the disease-causing mutation. What is the most likely mode of inheritance? Give an explanation.

AI Response

The most likely mode of inheritance is autosomal dominant with reduced penetrance.

- Reasoning:
- ○ III.2 is affected while being a heterozygote, so a single mutant allele is sufficient for disease → points to a dominant mutation.
- ○ I.1 is affected, but all individuals in generation II are unaffected, even though at least some of them must statistically have inherited the mutant allele if it's dominant.
- ○ For III.2 to be a heterozygote and affected while both parents in II appear unaffected, at least one parent must carry the mutant allele but not show the phenotype → this is classic reduced penetrance in an autosomal dominant trait.
- ○ X-linked dominant is unlikely because an affected male in generation I would be expected to pass the trait to all daughters, which is not seen here.

B **Copilot**



Researcher Prompt

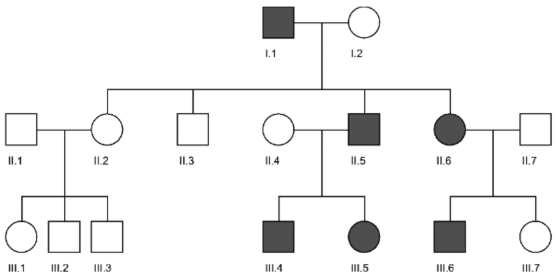
1- What is the most likely mode of inheritance for this pedigree?
a. X-linked recessive
b.X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
2-What is the degree of relative between III.1 and II.7
a.1st degree
b. 2nd degree
c.3rd degree
d.4th degree
e.Unrelated
3-What is the degree of relative between III.1 and II.8
a.1st degree
b.2nd degree
c.3rd degree
d.4th degree
e. Unrelated

AI Response

Most likely mode of inheritance:
c. Autosomal dominant
Degree of relationship between III.1 and II.7:
b. 2nd degree
Degree of relationship between III.1 and II.6:
b. 2nd degree

FIGURE 13: Panel A shows Copilot's response to Pedigree 7, and Panel B shows Copilot's response to Pedigree 8.

Copilot



Researcher Prompt

The following pedigree is for a family affected by an inherited blood disorder characterized by hemolytic anemia and recurrent painful episodes
1-What is the most likely disease
a.Sickle cell disease
b.G6PD deficiency
c.β-thalassemia
d.α-thalassemia
2-What is the likely mode of inheritance in this pedigree
a. X-linked recessive
b. X-linked dominant
c.Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
3- Based on this pedigree, explain how the mode of inheritance supports the most likely disease diagnosis.

AI Response

Most likely disease
Answer: a. Sickle cell disease
The combination of chronic hemolytic anemia and recurrent painful episodes (vaso-occlusive crises) is classic for sickle cell disease.
Likely mode of inheritance in this pedigree
Answer: c. Autosomal dominant
How the pedigree supports the mode of inheritance and diagnosis
Vertical transmission: Affected individuals appear in every generation, which is typical of an autosomal dominant pattern rather than a recessive one.
Both sexes affected equally: Males and females are affected in similar proportions, supporting an autosomal (not sex-linked) pattern.
Affected parent → affected children: In multiple matings, an affected parent with an unaffected partner has about half of the children affected, which fits an autosomal dominant trait.
Male-to-male transmission: An affected father has affected sons, which rules out X-linked inheritance and is consistent with autosomal inheritance.
Putting this together: the clinical picture strongly suggests a sickling hemoglobinopathy, and the pedigree pattern is most consistent with an autosomal dominant mode of inheritance in this family.

FIGURE 14: Copilot's response to Pedigree 9.

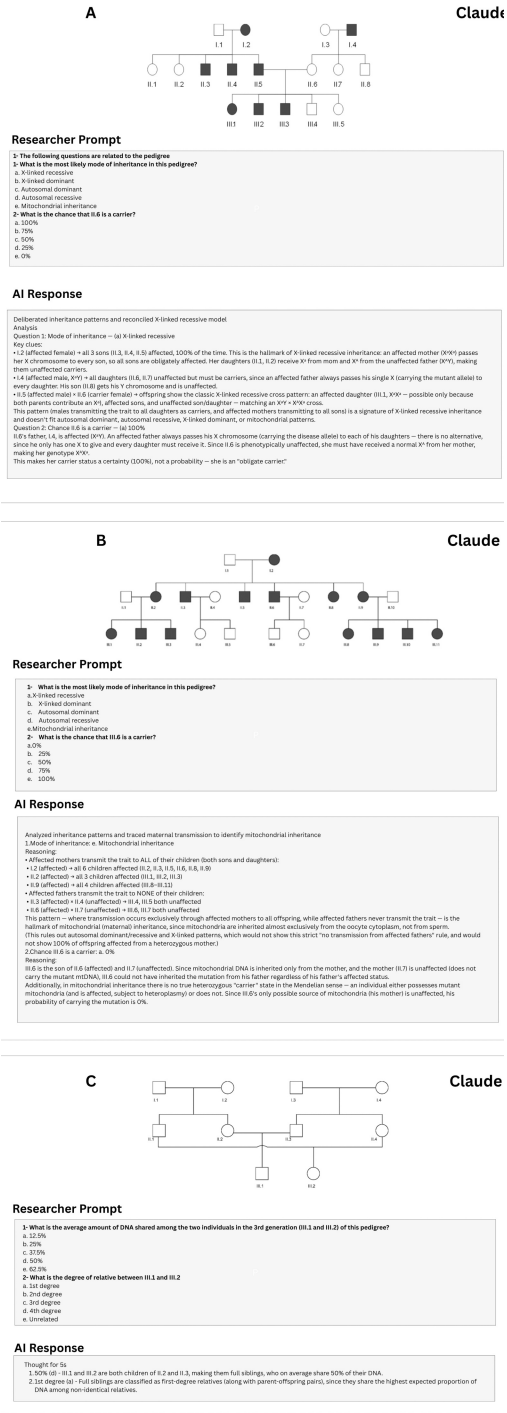
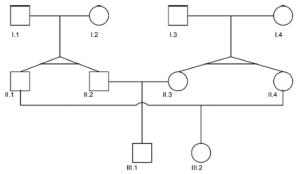


FIGURE 15: Panel A shows Claude's response to Pedigree 1, Panel B shows Claude's response to Pedigree 2. and Panel C shows Claude's response to Pedigree 3.

A **Claude**



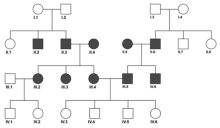
Researcher Prompt

The following questions are related to the pedigree
1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
a. 12.5%
b. 25%
c. 37.5%
d. 50%
e. 62.5%
2- What is the degree of relative between III.1 and III.2
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated

AI Response

Traced pedigree relationships to determine DNA sharing percentage
1.Average DNA shared between III.1 and III.2 — Answer: d. 50%
Looking at the pedigree, III.1 and III.2 are both children of the same couple (II.2 × II.3). This makes them full siblings. The lines running out to II.1 and II.4 simply show that these are the siblings (uncle/aunt) of II.2 and II.3, not additional parents — the actual mating (marriage) line producing III.1 and III.2 is the one joining II.2 and II.3.
Full siblings, on average, share 50% of their DNA (each parent contributes ~50% to each child, and on average half of that inherited material is identical between the two siblings).
2.Degree of relationship between III.1 and III.2 — Answer: a. 1st degree
First-degree relatives are those who share, on average, 50% of their DNA — this category includes:
• Parent–offspring pairs
• Full siblings
Since III.1 and III.2 are full siblings (same two parents: II.2 and II.3), they are classified as first-degree relatives, just like a parent and child would be, even though the biological relationship (siblings vs. parent-child) differs in nature.

B **Claude**



Researcher Prompt

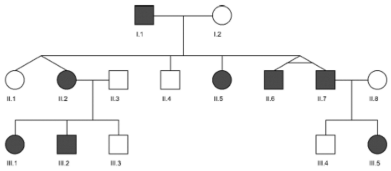
1- This pedigree is for a non-syndromic (congenital) deafness in humans that is inherited usually as an autosomal recessive condition. In the following pedigree, two deaf individuals, III.4 and III.5, have married and given birth to four children with normal hearing. Propose an explanation.
2- What are the chances for individuals IV.3, IV.4, IV.5, and IV.6 to be carriers?

AI Response

Analyzed genetic complementation explaining deaf parents' hearing children
1.Why two deaf parents (III.4 × III.5) have only normal-hearing children
The key is that "non-syndromic recessive deafness" is not caused by a single gene — there are many different genes (loci) in which a recessive mutation can independently cause deafness (this is called genetic/locus heterogeneity). Two deaf people can therefore be deaf because of mutations in different genes, not the same one.
Looking at the pedigree:
• III.4 comes from the family of II.3 × II.4 (both deaf), so she is homozygous recessive at one locus — call it gene A: genotype aa BB (normal, i.e., homozygous dominant, at locus B).
• III.5 comes from the family of II.5 × II.6 (both deaf), so he is homozygous recessive at a different locus — gene B: genotype AA bb (normal at locus A).
When III.4 (aa BB) and III.5 (AA bb) have children, each parent contributes:
• a normal dominant allele at the locus where they themselves are homozygous recessive (III.4 gives a normal "B", III.5 gives a normal "A")
• a mutant recessive allele at their own affected locus
So every child gets genotype Aa Bb — heterozygous at both loci. Since each child has at least one functional dominant allele for each gene, both genes work normally, and hearing is normal.
This phenomenon — two different recessive mutant genes "rescuing" each other's phenotype in the offspring — is called complementation, and it's the classic proof that two forms of a recessive trait (here, deafness) are caused by non-allelic (different) genes rather than the same gene.
2.Carrier probability for IV.3, IV.4, IV.5, and IV.6
Since III.4 is aa BB and III.5 is AA bb, this is essentially a cross:
aa BB × AA bb → all offspring Aa Bb
Every single child must inherit:
• one a allele from mom and one A from dad → Aa (carrier for gene A)
• one B allele from mom and one b from dad → Bb (carrier for gene B)
There is no possibility of any other genotype from this cross.
Answer: The probability that IV.3, IV.4, IV.5, and IV.6 are carriers is 100%. All four are obligate double heterozygotes (Aa Bb) — carriers for both forms of deafness — even though none of them is himself/herself deaf.

FIGURE 16: Panel A shows Claude's response to Pedigree 4, and Panel B shows Claude's response to Pedigree 5.

A **Claude**



Researcher Prompt

1- What is the most likely mode of inheritance in this pedigree?
a. X-linked recessive
b. X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
2- What is the most likely genotype of individual I.1 for the disease-causing mutation?

AI Response

Eliminated inheritance patterns through pedigree analysis systematically
1.Most likely mode of inheritance: (c) Autosomal dominant
Reasoning:
• The trait appears in every generation (I → II → III), consistent with a dominant pattern (recessive traits often skip generations).
• Affected × unaffected matings produce affected offspring of both sexes in roughly equal proportion (e.g., I.1 affected × I.2 unaffected → 4/6 affected children, including both affected sons and daughters).
• This rules out X-linked recessive, since an affected father (I.1) with an unaffected mother would not be expected to produce affected daughters (daughters would only be carriers).
• It also rules out X-linked dominant, because an affected father should transmit the trait to all his daughters and none of his sons (sons get his Y chromosome, not his X). Here, I.1 has affected sons (II.6, II.7), which is impossible under X-linked dominant inheritance.
• Autosomal recessive is unlikely because an affected individual (I.1) mating with an apparently unaffected individual (I.2) produces many affected children — this would require I.2 to be an unaffected carrier, and even so, you'd expect closer to 50% affected only if I.2 is heterozygous, which is possible, but recessive inheritance struggles to explain affected individuals in every single generation with unaffected-appearing spouses marrying in throughout (II.3, II.8) also having only some affected children in III — this fits a dominant, not recessive, pattern much better, especially with vertical transmission across 3 generations.
• Male-to-male transmission is also consistent (I.1 → II.6, II.7, both affected males), which further supports autosomal (rather than X-linked) inheritance, since X-linked traits cannot pass father-to-son.
2.Genotype of I.1:
I.1 is affected, so he carries at least one disease allele (let's call the dominant disease allele A and normal allele a).
Since I.1 (affected) × I.2 (unaffected, genotype aa) produced both affected and unaffected children (II.1 and II.4 unaffected; II.2, II.5, II.6, II.7 affected), I.1 cannot be homozygous dominant (AA), because an AA × aa cross would produce 100% affected offspring (all Aa).
Therefore, I.1 must be heterozygous: Aa
This is consistent with the ~50% affected : 50% unaffected ratio seen among his children, which is the expected outcome of an Aa × aa cross in autosomal dominant inheritance.

B **Claude**



Researcher Prompt

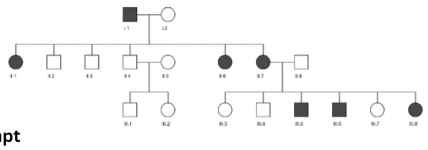
In this pedigree, III.2 is a heterozygote for the disease-causing mutation. What is the most likely mode of inheritance? Give an explanation.

AI Response

Reconciled inheritance pattern contradiction through incomplete penetrance hypothesis
Most likely mode of inheritance: Autosomal dominant with incomplete (reduced) penetrance
Reasoning
Why dominant, not recessive:
Since III.2 is affected while being heterozygous, a single copy of the mutant allele is sufficient to cause disease. This is the defining feature of a dominant trait (a recessive trait would require two copies/homozygosity to produce the phenotype).
Why autosomal, not X-linked:
I.1 is an affected male. If this were X-linked dominant, every daughter of I.1 would obligatorily inherit his mutant X allele and would be affected. However, II.1 and II.5 (his daughters) are both unaffected. This is inconsistent with X-linked dominant inheritance, so an autosomal locus fits the pedigree much better.
Why "incomplete penetrance" needs to be invoked:
If this is simple autosomal dominant inheritance, then II.3 must have inherited the mutant allele from his affected father (I.1) in order to pass it on to his affected daughter III.2 (since III.2's other parent, II.4, has no connection to the affected side of the family and is presumed non-carrier).
But II.3 himself shows no disease phenotype — he appears clinically unaffected despite (by inference) carrying the disease allele. This is the hallmark of incomplete penetrance: an individual carries the disease-causing genotype (heterozygous) but does not express the associated phenotype, allowing the trait to "skip" a generation (I.1 → affected; II.3 → silent carrier; III.2 → affected again).
Summary of the logic:
1. Heterozygous + affected → dominant
2. Affected father's unaffected daughters → rules out X-linked
3. Trait skips II.3 (obligate carrier) → incomplete penetrance
Conclusion: The pedigree is best explained by an autosomal dominant disorder with incomplete penetrance, where II.3 is a non-penetrant carrier who transmitted the mutant allele from I.1 to III.2.

FIGURE 17: Panel A shows Claude's response to Pedigree 6, and Panel B shows Claude's response to Pedigree 7.

A **Claude**



Researcher Prompt

1- What is the most likely mode of inheritance for this pedigree?
a. X-linked recessive
b. X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
2- What is the degree of relative between III.1 and II.7
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated
3- What is the degree of relative between III.1 and II.8
a. 1st degree
b. 2nd degree
c. 3rd degree
d. 4th degree
e. Unrelated

AI Response

1.Mode of inheritance: b. X-linked dominant
Reasoning: I.1 is an affected male. All of his daughters (II.1, II.6, II.7) are affected, while none of his sons (II.2, II.3, II.4) are affected — the hallmark of X-linked dominant inheritance (affected father → all daughters affected, no sons affected, since sons don't get his X). In the next generation, affected mother II.7 (heterozygous) transmits the trait to roughly half her children of both sexes (III.5, III.6, III.8 affected), which is exactly what's expected for X-linked dominant transmission from an affected mother. Autosomal dominant would also fit some of this, but the striking "all daughters affected/no sons affected" pattern from the affected father is the classic distinguishing clue for X-linked dominant.
2.III.1 and II.7: b. 2nd degree
III.1's father is II.4, who is the sibling of II.7. So II.7 is III.1's aunt — an aunt/uncle-niece/nephew relationship is a 2nd-degree relationship (~25% shared genes), the same category as grandparent-grandchild or half-siblings.
3.III.1 and II.8: e. Unrelated
II.8 married into the family (he is II.7's husband) and shares no blood/genetic relationship with II.4's line. Since III.1's connection to II.7's side comes only through marriage (II.8 is not a blood relative), III.1 and II.8 are genetically unrelated.

B **Claude**



Researcher Prompt

The following pedigree is for a family affected by an inherited blood disorder characterized by hemolytic anemia and recurrent painful episodes
1- What is the most likely disease
a. Sickle cell disease
b. G6PD deficiency
c. β-thalassemia
d. α-thalassemia
2- What is the likely mode of inheritance in this pedigree
a. X-linked recessive
b. X-linked dominant
c. Autosomal dominant
d. Autosomal recessive
e. Mitochondrial inheritance
3- Based on this pedigree, explain how the mode of inheritance supports the most likely disease diagnosis.

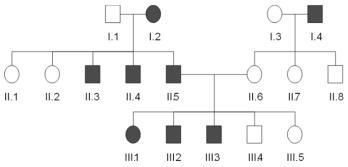
AI Response

Reconciled clinical presentation with inheritance pattern through population genetics
1.Most likely disease: (a) Sickle cell disease
The clinical description — hemolytic anemia plus recurrent painful (vaso-occlusive) episodes — is the classic textbook presentation of sickle cell disease. G6PD deficiency causes episodic hemolysis but not chronic painful crises; β- and α-thalassemia cause hemolytic anemia but not painful vaso-occlusive episodes.
2.Mode of inheritance: (d) Autosomal recessive
3.Explanation
At first glance the pedigree looks like it could be dominant, because an affected individual appears in every generation and unaffected × affected mating keeps producing affected offspring. But several features point specifically to autosomal recessive inheritance with pseudodominance, which actually strengthens the sickle cell diagnosis:
• Male-to-male transmission: I.1 (affected) has an affected son, II.5. A father passes only a Y chromosome to his son, so this single observation rules out any X-linked mode (recessive or dominant) — the gene must be autosomal.
• Both sexes equally affected: II.5 (male) and II.6 (female) are both affected, and their affected children include both sexes (III.4/III.6 males, III.5 female). This equal sex distribution is expected for an autosomal trait, not an X-linked one.
• "Unaffected" spouses marrying into the family are unaffected carriers, not homozygous normal: For a true autosomal dominant trait, an affected parent needs only one dominant allele to pass on. But sickle cell disease is caused by a recessive allele (HbS/HbS). The reason affected × "unaffected" matings (II.4 × II.5, II.6 × II.7) still produce affected children is that the incoming spouses (II.4, II.7) are themselves heterozygous carriers (AS), not homozygous normal — even though they show no disease phenotype. This is called pseudodominance: a recessive disease appears to be transmitted "dominantly" through successive generations because the carrier frequency is unusually high.
• Why carrier frequency would be high here: Sickle cell trait carriers have historically had a survival advantage against malaria, so in populations with malaria exposure (Sub-Saharan Africa, Mediterranean, Middle East, South Asia) the HbS allele frequency is high. This makes it statistically likely for an outside spouse marrying into an affected family to also be a carrier, especially when consanguineous or endogamous marriage is common — exactly the pattern that produces the pseudodominant appearance seen in generations II and III of this pedigree.
So the pedigree is consistent with autosomal recessive inheritance (I.1 = SS, I.2 = AS carrier; II.4 and II.7 = AS carriers), and the seemingly "vertical" transmission pattern is explained by pseudodominance rather than true dominance — fully compatible with sickle cell disease, which is molecularly known to be an autosomal recessive hemoglobinopathy.

FIGURE 18: Panel A shows Claude's response to Pedigree 8, and Panel B shows Claude's response to Pedigree 9.

Appendix 2

Pedigree 1

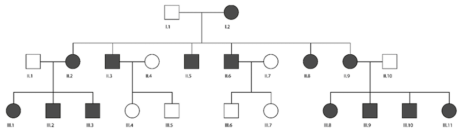


The following questions are related to the pedigree

1- What is the most likely mode of inheritance in this pedigree?
   a. X-linked recessive
   b. X-linked dominant
   c. Autosomal dominant
   d. Autosomal recessive
   e. Mitochondrial inheritance

2- What is the chance that II.6 is a carrier?
   a. 100%
   b. 75%
   c. 50%
   d. 25%
   e. 0%

Pedigree 2



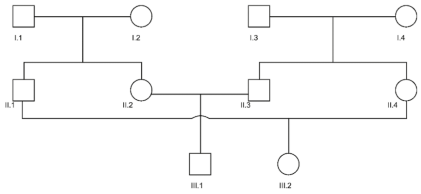
The following questions are related to the pedigree

1- What is the most likely mode of inheritance in this pedigree?
   a. X-linked recessive
   b. X-linked dominant
   c. Autosomal dominant
   d. Autosomal recessive
   e. Mitochondrial inheritance

2- What is the chance that III.6 is a carrier ?
   a. 0%
   b. 25%
   c. 50%
   d. 75%
   e. 100%

FIGURE 19: Answer key to Pedigree 1 & 2.

Pedigree 3

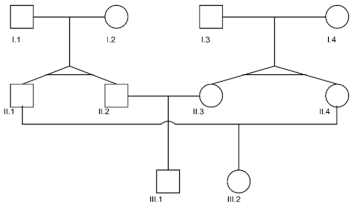


The following questions are related to the pedigree

1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
   a. 12.5%
   b. 25%
   c. 37.5%
   d. 50%
   e. 62.5%

2- What is the degree of relative between III.1 and III.2
   a. 1st degree
   b. 2nd degree
   c. 3rd degree
   d. 4th degree
   e. Unrelated

Pedigree 4



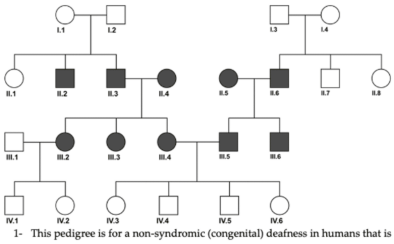
The following questions are related to the pedigree

1- What is the average amount of DNA shared among the two individuals in the 3rd generation (III.1 and III.2) of this pedigree?
   a. 12.5%
   b. 25%
   c. 37.5%
   d. 50%
   e. 62.5%

2- What is the degree of relative between III.1 and III.2
   a. 1st degree
   b. 2nd degree
   c. 3rd degree
   d. 4th degree
   e. Unrelated

FIGURE 20: Answer key to Pedigrees 3 & 4.

Pedigree 5



1- This pedigree is for a non-syndromic (congenital) deafness in humans that is inherited usually as an autosomal recessive condition. In the following pedigree, two deaf individuals, III.4 and III.5, have married and given birth to four children with normal hearing. Propose an explanation.

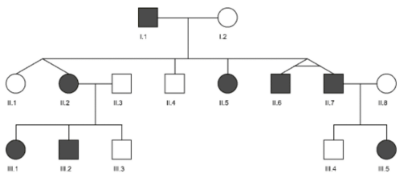
While both families have the non-syndromic deafness, which is inherited as an autosomal recessive disorder, each family has a different gene mutation responsible for the for their deafness. Therefore, each child from the parents (III.4 and III.5) will be heterozygous for the gene mutation of their parents. (meaning they will have one functional gene) and that is why they will not have the disease.

Example (No you don't need to memorize the gene names; understand the concept here)
III4 (Mom): Homozygous for mutation in *GJB2*, but normal *SLC26A4*
III.5: Homozygous for mutation in *SLC26A4*, but normal *GJB2*
Their children: Heterozygous for both genes; *GJB2*+/*GJB2*−, *SLC26A4*+/*SLC26A4*− leading to Normal hearing.

This explains how two deaf parents can have hearing children due to complementation of mutations in different genes located on different chromosomes.

2- What are the chances for individuals IV.3, IV.4, IV.5, and IV.6 to be carriers?
Correct answer is 100%

Pedigree 6



1- What is the most likely mode of inheritance in this pedigree?
   a. X-linked recessive
   b. X-linked dominant
   c. Autosomal dominant
   d. Autosomal recessive
   e. Mitochondrial inheritance

2- What is the most likely genotype of individual I.1 for the disease-causing mutation?
Correct answer is heterozygous

FIGURE 21: Answer key to Pedigrees 5 & 6.

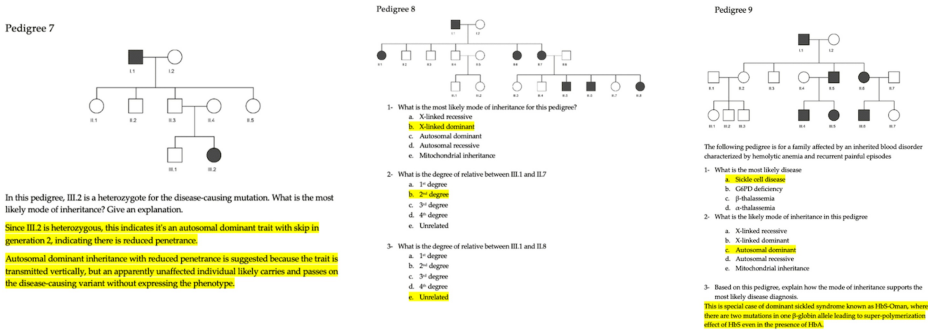


FIGURE 22: Answer key to Pedigrees 7, 8, and 9.

Additional Information

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All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Critical review of the manuscript for important intellectual content: Seba S. Abduljabbar, Mohammed Alqarni, Alawi Habara

Supervision: Alawi Habara

Disclosures

Human subjects: All authors have confirmed that this study did not involve human participants or tissue. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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