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Extended Kinship Inference. Part 2: Evaluation of the Impact of Information Loss on Likelihood Ratios and Haplotype Matching

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Abstract:	Medium-density single nucleotide polymorphism (SNP) profiles enable law enforcement to infer close and distant genetic relationships. Part one of this study demonstrated that the ForenSeq® Kintelligence Kit, which targets 10,230 SNPs, can facilitate extended kinship inference through kinship likelihood ratio (LR) and identical-by-descent (IBD) segment matching methods. However, if SNPs are not detected, or are incorrectly called, the ability to detect genetic relatives and accurately classify the relationship may be compromised. The Kintelligence profiles for the central individuals of two pedigrees described in Part One were edited to simulate information loss through locus and allele dropout. LRs were calculated with DBLR™ and SNP profiles were uploaded to GEDmatch PRO™ for database searching or direct comparison. The LRs decreased with increasing information loss but still provided strong statistical support for relatedness. LRs exceeded 100,000 for all full sibling to fifth degree relationships for up to 30% locus and allele dropout. Locus dropout did not significantly impact the ability to infer first to fifth degree relationships with IBD segment matching. Allele dropout had a greater impact, with 30% allele dropout impairing the ability to classify relationships to their correct degree. When allele dropout was greater than 10%, the fifth degree relative was no longer detected in the database search. This study highlights the robustness of LR calculations and the GEDmatch PRO™ IBD segment matching algorithms and the suitability of the Kintelligence Kit for medium-range kinship inference, with the algorithm maintaining the ability to infer relationships despite increasing information loss.

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Abstract:

Medium-density single nucleotide polymorphism (SNP) profiles enable law enforcement to infer close and distant genetic relationships. Part one of this study demonstrated that the ForenSeq® Kintelligence Kit, which targets 10,230 SNPs, can facilitate extended kinship inference through kinship likelihood ratio (LR) and identical-by-descent (IBD) segment matching methods. However, if SNPs are not detected, or are incorrectly called, the ability to detect genetic relatives and accurately classify the relationship may be compromised. The Kintelligence profiles for the central individuals of two pedigrees described in Part One were edited to simulate information loss through locus and allele dropout. LRs were calculated with DBLR™ and SNP profiles were uploaded to GEDmatch PRO™ for database searching or direct comparison. The LRs decreased with increasing information loss but still provided strong statistical support for relatedness. LRs exceeded 100,000 for all full sibling to fifth degree relationships for up to 30% locus and allele dropout. Locus dropout did not significantly impact the ability to infer first to fifth degree relationships with IBD segment matching. Allele dropout had a greater impact, with 30% allele dropout impairing the ability to classify relationships to their correct degree. When allele dropout was greater than 10%, the fifth degree relative was no longer detected in the database search. This study highlights the robustness of LR calculations and the GEDmatch PRO™ IBD segment matching algorithms and the suitability of the Kintelligence Kit for medium-range kinship inference, with the algorithm maintaining the ability to infer relationships despite increasing information loss.

Keywords:

Single nucleotide polymorphism; human identification; targeted amplicon sequencing; forensic investigative genetic genealogy; kinship.

Supplementary Material:

Figure S1. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual 1 with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated. **Figure S2**. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual 1 with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated. **Figure S3**. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual A with locus dropout ranging from 0 to 30% and the direct-to-consumer profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA. **Figure S4**. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual A with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA. **Figure S5**. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual 1 with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated. **Figure S6**. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual 1 with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated. **Figure S7**. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual A with allele dropout ranging from 0 to 30% and the direct-to-consumer profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA. **Figure S8**. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual A with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

1. Introduction

Extended kinship inference can be applied to forensic casework using single nucleotide polymorphism (SNP) profiles for the identification of persons of interest in criminal investigations and unidentified human remains in missing persons investigations.[1-3] However, forensic samples collected during an investigation may be degraded, inhibited or have low quantities of DNA. This can result in suboptimal DNA profiles being produced, limiting the ability to find direct or indirect matches (for short-range kinship testing) in a database or generate genetic intelligence, such as inferred biogeographical ancestry, externally visible characteristics or distant genetic relatives of the DNA donor.[4-7]

There are two common methods used to assess genetic relationships between individuals: kinship likelihood ratio (LR) calculations and identical by descent (IBD) segment matching. LRs provide statistical support for alternative propositions about the genetic relationship between two individuals based on the probabilities of observing alleles identical by state (IBS) in the DNA profiles.[2] IBD segment matching algorithms compare medium- and high-density SNP profiles to infer haplotypes or IBD segments that are shared between genetic relatives and co-inherited from a common ancestor.[1,8]

The ForenSeq® Kintelligence Kit (Verogen Inc., QIAGEN) targets 10,230 SNPs across the human genome in a medium-density targeted amplicon sequencing (TAS) panel.[6,9] The size of this panel facilitates kinship analysis using the LR calculation method or IBD segment matching using a database search or direct comparison.[8,10,11] Kintelligence profiles are compatible with upload to the law enforcement accessible genetic genealogy databases GEDmatch PRO™ and FamilyTreeDNA, allowing for comparison with over two million profiles uploaded by consenting members of the public on each database.[12,13] Part One of this study demonstrated Kintelligence profiles yielded LRs that provided very strong statistical support ($\log_{10}$ LR > 5) for relatedness between full siblings and fifth degree relatives.[14] The IBD segment matching tools on GEDmatch PRO™ were also able to detect all known first to fifth degree relatives available in the database.

Some studies have evaluated how locus dropout impacts kinship analysis for different SNP panels; however, further work is required to assess suboptimal profiles yielded from compromised forensic samples.[2,8,11] Partial profiles could appear as locus dropout, where loci are not detected during sequencing or fall below the analytical thresholds, or allele dropout, where a heterozygote is incorrectly called as homozygote. This paper presents Part Two of the study, which focuses on evaluating the Kintelligence profiles for central individuals of two pedigrees with simulated locus and allele dropout . This study aims to guide the interpretation of extended kinship inference results using LR calculations and IBD segment matching for partial profiles that could result from compromised forensic samples.

2. Methods

Ethics approval for this research was granted by the University of Technology (UTS) Human Research Ethics Committee (HREC) (UTS HREC NO. ETH21-5821 and amendment ETH21-6606). The methods for sample procurement, DNA extraction, quantification, library preparation, sequencing, LR calculation and IBD segment matching are described in Part One of this study.[14]

For the calculation of LRs for unrelated pairs of individuals (19 pairs), the first hypothesis (H_1) proposed a relationship ranging from first (parent/offspring or full sibling) to eighth degree relationships and the alternative hypothesis (H_2) proposed that the individuals were unrelated. For the genetically related pairs of individuals, H_1 proposed the true relationship of the individuals and H_2 proposed that they were unrelated. The statistical support for the hypotheses is presented using the verbal scale based on the $\log_{10}$ LR results (Table 1).~~The verbal scale for statistical support provided by $\log_{10}$ LR results is provided in Table 1.~~

Pedigree Group 1 (Individuals 1 – 12) provided buccal swabs for DNA profiling with the Kintelligence Kit (Figure 1). Pedigree Group 2 (Individuals A – L) provided the kit numbers for pre-existing DTC data uploaded to GEDmatch™ and the central individual (Individual A) provided a buccal swab for DNA profiling with the Kintelligence Kit (Figure 2; Table 2).[1] All Kintelligence profiles were uploaded to GEDmatch PRO™ as laboratory validation samples.

For both pedigrees, the Kintelligence profiles of the central individual (Individual 1 from Pedigree Group 1; Individual A from Pedigree Group 2) were manually edited using the Universal Analysis Software (UAS) (Verogen, Inc.) to simulate varying degrees of locus and allele dropout. Table 3 outlines the call rates and autosomal heterozygosity for the generated Kintelligence profiles. Call rates were calculated as the number of typed SNPs out of a possible 10,230 SNPs for Individual 1 (male) and 10,145 SNPs for Individual A (female). Autosomal heterozygosity was calculated as the proportion of typed autosomal SNPs (up to 10,039 SNPs) that were heterozygous.

Locus dropout was assessed in increments of 5% with a minimum call rate of 70% generated for the profiles. SNPs were removed based on the frequency of locus dropout as observed by [10].[10] After this list of SNPs was exhausted, SNPs were removed by increasing the total coverage threshold required to call a SNP. Allele dropout was calculated as the proportion of heterozygous autosomal SNPs that were called as heterozygous and changed to homozygous, across the testing range of 5% to 30% allele dropout. The minor allele of each heterozygous SNP was removed from the final genotype.

3. Results

3.1. Impact of Locus Dropout

3.1.1. LR Calculations Between Kintelligence Profiles (Pedigree Group 1)

Increasing locus dropout in the Kintelligence profile of Individual 1 resulted in the $\log_{10}$ LRs decreasing for all relationships greater than the first degree tested within Pedigree Group 1 (Figure 3). The results for the first degree relationships were unaffected by locus dropout. As noted in Part One, when a relationship is impossible (LR = 0), the $\log_{10}$ LR results are given as negative infinity ($-\infty$).[15] Alternatively, DBLR™ does not report $\log_{10}$ LRs that exceed 300 (LR > 10^{300}) and return the $\log_{10}$ LR as infinite (∞).

The parent/offspring relationship (Individual 2) produced a $\log_{10}$ LR of $-\infty$, inferring the relationship was impossible, for all levels of dropout due to the profiles failing to have at least one allele in common at every SNP. The full sibling relationship (Individual 3) was not observably impacted by locus dropout, with the LRs exceeding 10^{300} and remaining incomputable by DBLR™, returning a $\log_{10}$ LR of ∞ and inferring H_2 was impossible. The greatest decrease was observed in the second degree relationships (Individual 4 and Individual 5). For locus dropout ranging from 0% to 30%, the $\log_{10}$ LR decreased from 232 to 160 for Individual 4 and from 250 to 176 for Individual 5. This represented an average decrease

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[1] The use of DTC data for research was in compliance with the terms and conditions at the time the respective data were downloaded by the volunteers. All volunteers were notified at the conclusion of the study so they could opt out of law enforcement searching or remove their DNA data from GEDmatch™ to ensure that future use of their data is in compliance with their preferences and relevant terms and conditions.

of 12 in the $\log_{10}$ LR for every 5% of SNPs lost. However, these values all provided very strong statistical support for H_1 and the decreases in $\log_{10}$ LRs with locus dropout do not have any practical significance.

For the third degree relationships (Individual 6, Individual 7 and Individual 8), the $\log_{10}$ LR decreased steadily by approximately 7.2 for every 5% interval of locus dropout tested (Figure 3). The exception was Individual 8, which saw the $\log_{10}$ LR increase from 86 to 88 when the call rate of Individual 1 was first reduced to 95%.

For the fourth and fifth degree relationships (Individual 9 and Individual 10, respectively), a small decrease in the $\log_{10}$ LR was observed with increasing locus dropout. For the fourth degree relationship, the $\log_{10}$ LR decreased from 43 to 28, with an average loss of 2.5 per 5% increment of locus dropout. The $\log_{10}$ LRs decreased by an average of 1.4 per 5% increment for the fifth degree relationship, from 22 to 17, still providing very strong statistical support for relatedness.

The seventh degree relationship (Individual 11) provided very strong statistical support for the proposed relationship when there was no locus dropout ($\log_{10}$ LR = 5.2). However, locus dropout resulted in a substantial drop in statistical support for relatedness when the call rate dropped to 70%, producing a $\log_{10}$ LR of 0.92,. This means that, at this level of dropout, it is only 8.35 times more likely to observe these Kintelligence profiles if the individuals are seventh degree relatives than if they are unrelated. This was not distinguishable from the $\log_{10}$ LRs obtained from testing unrelated pairs of individuals.

When calculating the kinship LRs between the Individual 1 profiles and the unrelated individual (Individual 12), the $\log_{10}$ LRs increased as the rate of locus dropout increased (Figure 4). However, this increase plateaued for all relationship degrees at 20% locus dropout. When testing H_1 for first to fourth degree relationships, there was very strong statistical support for H_2, consistent with the true unrelated status of this pair. When testing H_1 for fifth to seventh degree relationships, only limited to moderate statistical support was provided for H_2. Positive $\log_{10}$ LRs that statistically supported H_1 were produced for fifth degree at 20% locus dropout and greater, sixth degree at 15% locus dropout and greater and seventh degree at 10% locus dropout and greater. The strongest statistical support for an incorrect inference of relatedness occurred at 20% locus dropout, where H_1 proposed a sixth degree relationship with a $\log_{10}$ LR of 1.5. The $\log_{10}$ LRs when testing H_1 for fifth to seventh degree relationships could not be distinguished from the results obtained from true seventh degree relationships when locus dropout was greater than 10%.

3.1.2. IBD Segment Matching Between Kintelligence Profiles (Pedigree Group 1)

For the first to fourth degree relationships, all appeared in either the high confidence or expanded match lists for all levels of locus dropout tested. For Individual 1 profiles with call rates from 70 to 85%, the fifth degree relationship (Individual 10) results did not appear in the high confidence match list and only appeared in the expanded match list. The seventh degree relationship (Individual 11) and the unrelated individual (Individual 12) were not detected in the database search and were directly compared to Individual 1 using the One-to-One Kintelligence DNA Comparison tool.

As locus dropout increased, additional matches were identified by the One-to-Many Kinship tool that were not known genetic relatives of Individual 1 (Figure 5). Very few of these matches were listed in the high confidence match list and those that were had an estimated shared cM over 200 (average: 205 ± 1 cM). The additional matches in the expanded match list had an average estimated shared cM of 160 ± 5 cM. No additional matches appeared in the high confidence match list when locus dropout was less than 15% or at 25% locus dropout. With the exception of the 25% locus dropout test, the number of additional matches in the extended match list increased as locus dropout increased. Furthermore, these additional matches tended to appear in the match list for the next level of locus dropout tested.

The Individual 1 profiles with lower call rates were able to match to the Individual 1 Kintelligence profiles with varying levels of locus dropout (0 – 30%) in the One-to-Many Kinship tool as likely “self”, regardless of the number of SNPs being compared. All 21 pairwise comparisons resulted in high estimated shared cM values, with an average of 6,559 ± 4 cM. These values all fell within the range provided by GEDmatch PRO™ as likely to be self (6464 – 6684 cM).

There was minimal variability in the estimated shared cM for the relationships tested in Group 1 as locus dropout increased (Figure 6). The standard deviations for the estimated shared cM values were calculated across the locus dropout tests for each individual and averaged to calculate the overall variance. The overall variance for the estimated shared cM values was 29.3 cM.

The average IBD segment length decreased with increasing locus dropout for first degree relationships (Individual 2 and Individual 3) and increased for the second degree relationships (Individual 4 and Individual 5; Figure S1). There was no discernible impact of locus dropout on the average IBD segment lengths for the other relationships. The overall variance in the average segment length was 2.9 cM.

The number of IBD segments detected by the algorithm increased with locus dropout for Individual 2, Individual 3, Individual 8, Individual 9 and Individual 10 but decreased for Individual 5 (Figure S2). The greatest impact of locus dropout on the number of IBD segments detected occurred for the parent/offspring relationship (Individual 2), where five additional segments were identified across the locus dropout range, and for the second degree relationship (Individual 5), which lost five segments (Figure S2). The overall variance in the number of IBD segments detected was 1.1 segments.

The unrelated individual (Individual 12) could not be distinguished from the seventh degree relationship (Individual 11) when considering the estimated shared cM and the average length and number of IBD segments detected. A single IBD segment was detected between Individual 1 and Individual 12 on chromosome 4 (24.5 cM) that dropped out at 15% locus dropout. A different IBD segment was detected on chromosome 13 at 20% locus dropout (24.1 cM) that increased in size for 25% and 30% locus dropout (43.1 cM), and a second IBD segment only appeared when testing 25% locus dropout on chromosome 14 (22.5 cM).

3.1.3. IBD Segment Matching Between Kintelligence and DTC Kits (Pedigree Group 2)

As observed with Pedigree Group 1, there was minimal variability in the results when comparing Individual A with varying degrees of locus dropout and the DTC profiles from Pedigree Group 2. The majority of DTC kits from genetically related individuals were included in the high confidence or expanded match lists. Only the Individual A 23andMe kit did not appear in the One-to-Many Kinship results at 30% locus dropout, as fewer than 6,000 overlapping SNPs were detected, failing to meet the threshold for inclusion in the database match list. Despite this, the direct comparison of this kit to the Individual A Kintelligence profile produced results that were consistent with all other DTC kits for Individual A.

All IBD segment matching results were consistent between the different types of relationships tested, as well as between the DTC kits for each individual. Locus dropout did not significantly impact the estimated shared cM (Figure 7). The average IBD segment length and number of IBD segments detected decreased with increasing locus dropout for some individuals while increasing for others (Figure S3 and Figure S4, respectively). The overall variances across locus dropout tests were 25.2 cM for the estimated shared cM, 3.4 cM for the average IBD segment lengths and 1.3 for the number of IBD segments.

The greatest degree of variability in results due to increasing locus dropout was observed in the number of IBD segments detected (Figure S4). For the parent/offspring relationship (Individual C), several IBD segments were lost, with the AncestryDNA kit decreasing by five segments and the FamilyTreeDNA kit by only two segments. IBD segments were lost for both kits for one full sibling relationship (Individual G) after additional IBD segments were detected at 15% locus dropout for the AncestryDNA kit and 5% for the FamilyTreeDNA kit; by 30% locus dropout, the number of IBD segments detected for the AncestryDNA kit decreased by five segments, whereas the FamilyTreeDNA kit decreased by only two segments. In contrast, for the full sibling relationship (Individual I), additional IBD segments were detected as locus dropout increased, with the AncestryDNA kit increasing by six segments and the FamilyTreeDNA kit by five segments.

The unrelated individual (Individual L) had only a single IBD segment detected (28.2 cM) when compared to the full Individual A Kintelligence profile. However, this segment was not detected when comparing Individual L to any of the profiles with locus dropout.

3.2. Impact of Allele Dropout

3.2.1. LR Calculations Between Kintelligence Profiles (Pedigree Group 1)

The $\log_{10}$ LR decreased with increasing allele dropout of the Individual 1 profile (Figure 8). As observed in the locus dropout study, the impact of allele dropout on the $\log_{10}$ LRs for the first degree relationships was unable to be evaluated. The $\log_{10}$ LRs remained at ∞ for the full sibling relationship (Individual 3) as $\log_{10}$ LRs exceeding 300 are not reported by DBLR™. As there was already allele dropout observed in the comparison of full profiles for the parent/offspring relationship (Individual 2), the $\log_{10}$ LRs were represented as -∞, inferring the relationship was impossible. The second degree relationships showed the greatest rate of decrease in $\log_{10}$ LRs at an average of 22.5 between each 5% increment of allele dropout tested, with those from Individual 4 decreasing from 232 to 111 and those from Individual 5 decreasing from 250 to 176.

The $\log_{10}$ LRs decreased in a similar pattern for the third degree relationships (Individual 6, Individual 7 and Individual 8), with minimal change between 15% and 20% allele dropout and between 25% and 30% allele dropout. While Individual 6 and Individual 7 produced similar values, the $\log_{10}$ LRs for Individual 8 were lower but still provided very strong statistical support for relatedness. The $\log_{10}$ LR for the fourth degree relationship (Individual 9) decreased from 43 to 11, with an average reduction of 5.3 per 5% increment of allele dropout. The $\log_{10}$ LR for the fifth degree relationship (Individual 10) decreased from 22 to 4.7 at 30% allele dropout, but still provided strong statistical support for H_1. Finally, the $\log_{10}$ LRs calculated for the seventh degree relationship (Individual 11) decreased from 5.2 at 0% allele dropout to being uninformative, where a $\log_{10}$ LR is at 0 and neither hypothesis is supported, at 15% allele dropout ($\log_{10}$ LR = 0.1) and provided limited statistical support for H_2 at 30% allele dropout ($\log_{10}$ = -0.5).

For the unrelated individual (Individual 12), allele dropout resulted in a decrease in the $\log_{10}$ LR (Figure 9). The highest $\log_{10}$ LR across all tests was the H_1 proposition for a seventh degree relationship with no allele dropout ($\log_{10}$ LR = -0.1), which provided limited statistical support for H_2. All first to fourth degree relationship tests provided very strong statistical support for H_2, and only limited to moderate statistical support for H_2 for fifth to seventh degree relationships.

3.2.2. IBD Segment Matching Between Kintelligence Profiles (Pedigree Group 1)

In contrast to the locus dropout study, a gradual decrease was observed in almost all results obtained from the IBD segment matching algorithm with increasing allele dropout. Allele dropout resulted in the more distant genetic relatives not being included in the match lists when searching the database. The fifth degree relationship (Individual 10) did not appear in the high confidence or expanded match lists using the One-to-Many Kinship tool when allele dropout exceeded 10%. As a result, the remaining comparisons for the fifth degree relationship were performed using the One-to-One Kintelligence DNA Comparison tool. Similarly, the comparisons for the seventh degree relationship (Individual 11) and unrelated individual (Individual 12), across all degrees of allele dropout tested, were conducted using the One-to-One Kintelligence DNA Comparison tool.

No additional matches were included in the high confidence match list that were not already known genetic relatives of Individual 1. However, several additional matches were observed in the expanded match list, with fewer than ten matches for each version of the profile with varying allele dropout (Figure 10). The average estimated shared cM for these matches was 139 ± 4 cM. The number of additional matches did not correlate with the allele dropout rate and the matches did not appear in any other match lists for different levels of allele dropout tested.

When comparing the full Kintelligence profile to those with increasing amounts of allele dropout, the estimated shared cM values showed a sharp decline after 5% allele dropout (Table 4). At 5% allele dropout, the estimated shared cM remained within the range provided by GEDmatch PRO™ for self (6464 – 6684 cM) but decreased and plateaued around 3400 cM after 10% allele dropout. This suggests that, beyond 5% dropout, the profiles are more likely to represent first degree relatives rather than originating from the same individual. Despite this decrease in shared cM, the number of IBD segments (22) and average IBD segment length (152 cM) remained consistent across the comparisons and allows for differentiation between self with allele dropout and true parent/offspring relationships. However, there were increasing numbers of SNPs where both alleles were not in common between the profiles, resulting in the decreased estimated shared cM. For all 21 pairwise comparisons of Individual 1 profiles, the estimated shared cM values were within the range for self if the allele dropout rates were within 5% (Table 4).

Figure 11 illustrates the gradual decrease in the estimated shared cM between Individual 1 and the individuals in Pedigree Group 1 as allele dropout increased. There was no observable impact on the parent/offspring relationship (Individual 2), with a variance of 35.6 cM. In contrast, the full sibling relationship (Individual 3) showed a decrease in the estimated shared cM from an average of 2530 ± 40 cM (0 – 15% allele dropout) to 2298 cM at 20%, dropping below the range for first degree relationships (2328 – 3065 cM). The estimated shared cM decreased for second degree relationships (Individual 4 and Individual 5) after 20% allele dropout, falling within the range for third degree relationships (448 – 1081 cM) at 30% allele dropout.

There was greater variability observed in the third degree relationships. The estimated shared cM for Individual 7 remained stable until 30% allele dropout, while the estimated shared cM values for Individual 6 decreased from an average of 686 ± 30 (0 – 15% allele dropout) to 522 ± 6 cM (20 – 30% allele dropout). However, Individual 8 produced consistent results up to 20% allele dropout (average = 600 ± 29 cM) before dropping sharply to 143 cM, the greatest decrease observed across all allele dropout tests.

Overall, allele dropout had minimal impact on the estimated shared cM values for relationships of fourth degree and greater, except when no IBD segments were detected, i.e. no estimated shared cM (Figure 11). The estimated shard cM for the fourth degree relationship (Individual 9) steadily increased from 285 cM (0% allele dropout) to a peak of 357 cM (15% allele dropout), before decreasing to 169 cM

(30% allele dropout). Despite not appearing in the match lists, there was minimal variability observed in the estimated shared cM for the fifth degree relationship (Individual 10, variance = 46.6 cM) and seventh degree relationship (Individual 11, variance = 16.8 cM). However, at 30% allele dropout, no IBD segments were detected for the seventh degree relationship.

The single IBD segment detected between the Individual 1 and the unrelated individual (Individual 12) on chromosome 4 (24.5 cM) was identifiable when testing the Kintelligence profile with 0% to 10% allele dropout. At higher levels of allele dropout, no IBD segments were detected and the estimated shared cM was 0.

The average length of the IBD segments typically increased with increasing allele dropout for several relationships (Figure S5). This trend was observed in the full sibling (Individual 3), a second degree (Individual 4), some third degree (Individual 6 and Individual 7) and the fourth degree (Individual 9) relationships. However, there was minimal variability observed in the parent/offspring (Individual 2), other second degree (Individual 5) and seventh degree (Individual 11) relationships, until no IBD segments were detected at 30% allele dropout for the latter. An exception was Individual 8, which showed an increase in the average IBD segment length up to 20% allele dropout before dropping at 25%. The overall variance in the average IBD segment length across all relationships tested was 5.4 cM.

Increasing allele dropout generally resulted in fewer IBD segments shared between relatives being detected (Figure S6). However, the parent/offspring (Individual 2) and fourth degree (Individual 9) relationships showed a greater number of IBD segments being detected with increasing allele dropout. For the former, an additional six IBD segments were detected across the allele dropout range tested. The latter saw a large increase of nine IBD segments from 0% to 20% allele dropout, before dropping to only four IBD segments at 30% allele dropout. Excluding these individuals, the overall variance in the number of IBD segments detected was 2.6 segments.

3.2.3. IBD Segment Matching Between Kintelligence and DTC Kits (Pedigree Group 2)

Similar trends to those observed in Pedigree Group 1 were seen when comparing the Kintelligence profile of Individual A with varying amounts of allele dropout and the DTC kits from Pedigree Group 2. There was a greater impact of allele dropout on the results than for locus dropout. All DTC kits from the true genetic relatives were detected in the high confidence or expanded match lists using the One-to-Many Kinship tool; only the unrelated individual (Individual L) was not detected in the database search and required direct comparison using the One-to-One Kintelligence DNA Comparison tool.

When comparing the Kintelligence profile to the DTC kits for Individual A, there was no observable impact of 5% allele dropout on the estimated shared cM (Figure 12). However, after this, the estimated shared cM decreased substantially until plateauing at approximately 3400 cM when allele dropout was 15% or higher. This result was similar to those of the Individual 1 Kintelligence profiles, indicating that the relationship between the Individual A profiles was more likely to be of the first degree rather than self. Despite the impact on the estimated shared cM between Individual A profiles, no variation was observed in the average length of IBD segments (152 cM; Figure S7) or the number of IBD segments (22 segments; Figure S8) with increasing allele dropout. Both the average length and number of IBD segment results support that the relationship is self with allele dropout as opposed to a parent/offspring relationship.

There was a decrease in the estimated shared cM when comparing the Individual A Kintelligence profiles to the DTC kits of the first and second degree relatives with increasing allele dropout (Figure 12). The relationship with the least variability across the range of allele dropout was a parent/offspring relationship (Individual B, variance = 30.4 cM), with no differences observed between the different DTC kits. The other parent/offspring relationships decreased by approximately 200 cM once allele dropout exceeded 25%, bringing the overall variance for parent/offspring relationships to 92.7 cM. There was a steady decrease in the estimated shared cM values for full sibling relationships with increasing allele dropout. Individual G had the greatest reduction, with an average loss of 138 cM for every 5% interval of allele dropout tested. There was no observable impact for one of the second degree relationships (Individual J); however, the estimated shared cM for the other second degree relationship (Individual K) steadily decreased by 127 cM per 5% interval of allele dropout, before dropping by 303 cM between 25% and 30% allele dropout.

There was generally low variability in the relationships for the average length of IBD segments with an overall variance of 3.3 cM (Figure S7). The number of IBD segments showed a general decrease with increasing allele dropout and had an overall variance of 1.6 segments (Figure S8). Furthermore, no difference were observed between the DTC kits for each individual. The greatest variability in the average length of IBD segments was observed in the parent/offspring relationships, while there was a slight increase in the average segment length for full sibling relationships and a second degree relationship (Individual K; Figure S7).

There were two individuals where allele dropout impacted the number of IBD segments detected (Figure S8). The results for both DTC kits for Individual G varied; the first 5% of allele dropout caused the loss of six IBD segments for the AncestryDNA kit that were not lost for the FamilyTreeDNA kit and up to four IBD segments were lost for each 5% interval. Individual K also showed a loss of IBD segments with increasing allele dropout, losing up to four IBD segments per 5% increment and a total of 16 IBD segments by 30% allele dropout.

4. Discussion

The Kintelligence Kit is a robust panel capable of producing extended kinship inferences with both LR calculations and IBD segment matching algorithms, even with suboptimal partial profiles. When testing locus and allele dropout, both kinship inference methods produced sufficient statistical support for relatedness, extending to fifth degree relationships (e.g. second cousins). Both methods allow for direct comparison of DNA profiles between putative genetic relatives and the windowed kinship algorithm on GEDmatch PRO™ facilitates IBD segment matching for medium-density SNP profiles, enabling the identification of possible genetic relatives present in the database. In cases where other forensic techniques are unable to provide an identification, extended kinship inference can provide law enforcement with investigative leads. This method is particularly useful beyond the short-range kinship inference offered by short tandem repeat (STR) profiles, which are typically limited to first degree relationships.

The LR calculations were negatively impacted by both forms of information loss tested in this study, but still provided at least very strong statistical support ($\log_{10}$ LR > 5) for all full sibling to fifth degree relationships.[16] For both the locus and allele dropout studies, the parent/offspring relationship could not be calculated, as there had to be at least one allele in common at every SNP. This was also the case in Part One of this study, and the application of a probabilistic model is recommended to account for genotyping error due to the large size of the Kintelligence panel.[14] The ability to infer the full sibling relationship was not practically impacted by locus or allele dropout. As the $\log_{10}$ LRs exceeded 300, DBLR™ returned the $\log_{10}$ LR at ∞ for all full sibling tests. The first to fifth degree relationships were able to be differentiated from the unrelated individual for all levels of locus and allele dropout tested in this study. However, the seventh degree relationship could not be distinguished from the unrelated individual once locus dropout exceeded 20% or allele dropout exceeded 10%.

Partial medium-density SNP profiles have been evaluated for the impact of locus dropout on LR calculations in previous studies.[2,11] [11] observed a median $\log_{10}$ LR of approximately 780 for first degree, 200 for second degree, 70 for third degree, 30 for fourth degree and 5 for fifth degree relationships using simulated partial Kintelligence profiles.[11] The results generated in this study with Pedigree Group 1 supported these findings for second to fourth degree relationships but produced $\log_{10}$ LRs exceeding 300 for full siblings and $\log_{10}$ LRs exceeding 13 for fifth degree relationships. This indicates very strong statistical support for all full sibling to fifth degree relationships tested with up to 30% locus dropout. In contrast, 97% of fourth degree and 81% of fifth degree relationships produced LRs that provided strong statistical support ($\log_{10}$ LR > 4) in the study by [11].[11,16]

Locus dropout was also evaluated by [2] when constructing a 6,600 SNP panel for extended kinship inference.[2] By reducing the original panel of approximately 10,000 SNPs to 6,600, the $\log_{10}$ LRs decreased for real-world third and fifth degree relatives by approximately half. This magnitude of loss in the statistical support for relatedness was similar to the findings in this study when testing the loss of 30% of available SNPs in the Kintelligence Kit. However, both of these other studies only assessed locus dropout as a factor influencing extended kinship inference.[2,11] In contrast, this study observed that allele dropout had a greater impact on the LR calculations and it is likely that Kintelligence profiles obtained from compromised forensic samples will likely contain a combination of both locus and allele dropout. Despite 30% of heterozygous SNPs being incorrectly called as homozygous, all $\log_{10}$ LRs for full sibling to fifth degree relationships exceeded 5, providing very strong statistical support for relatedness.[16]

The results obtained from IBD segment matching were less impacted by information loss than the LR calculations. Locus dropout had no observable impact on the ability to infer relatedness with up to 30% loss of the profile and first to fifth degree relatives could be differentiated from unrelated individuals at all levels of locus dropout tested. When the call rate of a Kintelligence profile is less than 70%, the profile is no longer compatible with upload to GEDmatch PRO™.[12] This limit was recommended by [8] in the development of the windowed kinship algorithm, which tested locus dropout at intervals of 2,000 SNPs.[8] Their simulations found that locus dropout could not exceed 20% to reliably infer fifth degree relationships, 40% for fourth degree relationships and 60% for third degree relationships.[8] This study observed that the fifth degree relationship was still detectable at 30% locus dropout, but there was a greater number of potential matches listed in the database search that were not known genetic relatives.

Similar to the LR calculations, allele dropout had a greater impact on IBD segment matching but did not significantly impair the ability to detect first to fourth degree relationships and differentiate them from unrelated individuals, with only the fifth degree relative failing to appear in the database match list after 10% allele dropout. Allele dropout also complicated the ability to distinguish profiles originating from the same person from those of their first degree relatives; however, the average length and number of IBD segments can assist with differentiating self from a parent/offspring relationship as these values did not vary with allele dropout. [8] simulated 5% to 100% allele dropout on the windowed kinship algorithm and concluded that the results were sufficient to infer first to third degree relationships up to 20% allele dropout and first to second degree relationships up to 40%.[8] However, the specificity of extended kinship inference was not impacted and false positives were not introduced by reducing profile heterozygosity.[8] These findings were supported by the present study, where fewer than ten matches were returned that were not known genetic relatives of the individual.

Furthermore, there were consistent findings between Pedigree Group 1 and Pedigree Group 2 for the first and second degree relationships, as well as comparisons to known unrelated individuals. This indicates that comparing Kintelligence profiles with either DTC kits uploaded by the public or other Kintelligence profiles does not impact the results.

5. Conclusions

This study demonstrated that partial medium-density SNP profiles generated with the Kintelligence Kit are suitable for extended kinship inference using both LR calculation or IBD segment matching. While both methods were impacted by information loss, allele dropout had a greater effect than locus dropout. Despite this, first to fifth degree relationships could still be detected and differentiated from unrelated individuals with the maximum dropout levels applied. LR calculations provided strong statistical support for full siblings to fifth degree relatives, excluding parent/offspring relationships where an allele must be in common at every SNP. The performance of the windowed kinship algorithm on GEDmatch PRO™ was maintained across all levels of locus dropout tested, whereas the accuracy of IBD segment matching results decreased with increasing allele dropout. Both extended kinship inference methods can therefore be employed for forensic samples that produce partial Kintelligence profiles.

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Table 1. Verbal scale for $\log_{10}$ LR results and the statistical support for each hypothesis.[16]

$\log_{10}$ LR	**Interpretation**
≤ –5	Very strong statistical support for H_2
–4	Strong statistical support for H_2
–3	Moderately strong statistical support for H_2
–2	Moderate statistical support for H_2
–1	Limited statistical support for H_2
0	Uninformative
1	Limited statistical support for H_1
2	Moderate statistical support for H_1
3	Moderately strong statistical support for H_1
4	Strong statistical support for H_1
≥ 5	Very strong statistical support for H_1

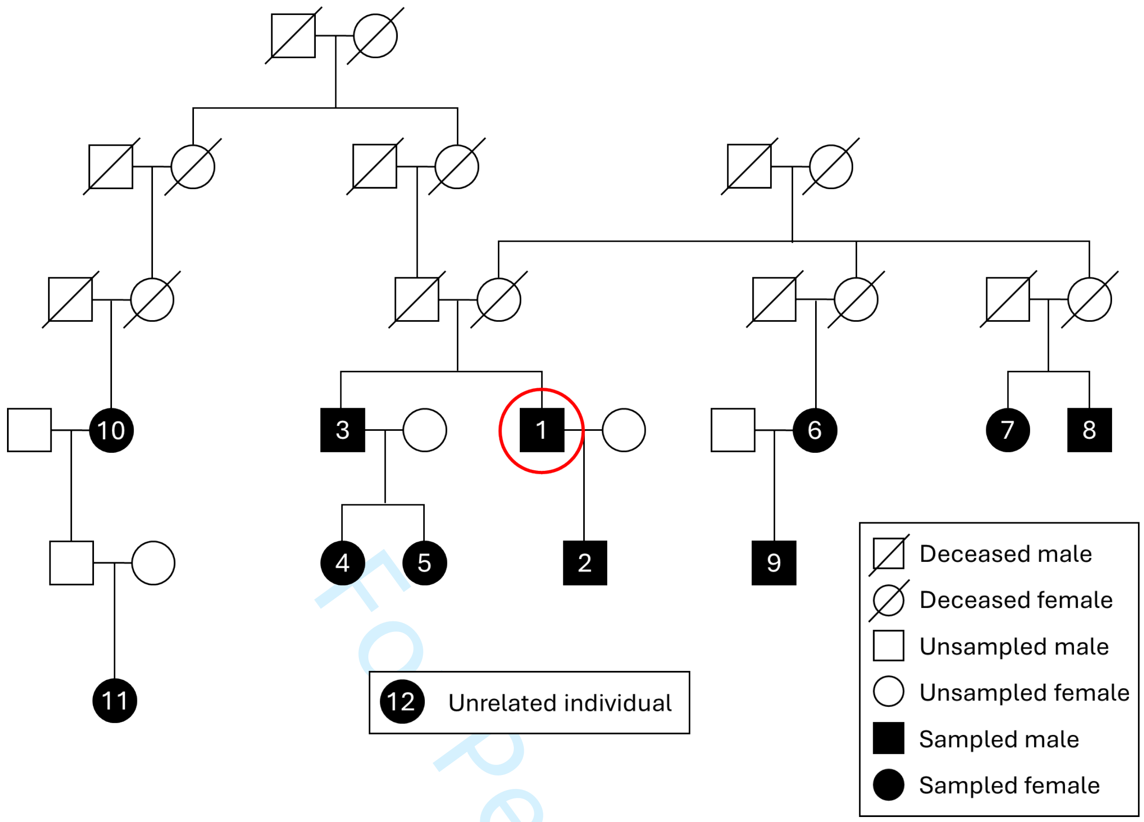

Figure 1. Pedigree Group 1, with numbers corresponding to Individuals 1 through 12.[14] *Individuals included in the study are filled in (black), with living relatives linking the family members not filled (white). Deceased relatives are crossed out. Individual 12 is unrelated to all individuals in the group. The central individual (Individual 1) is circled in red.*

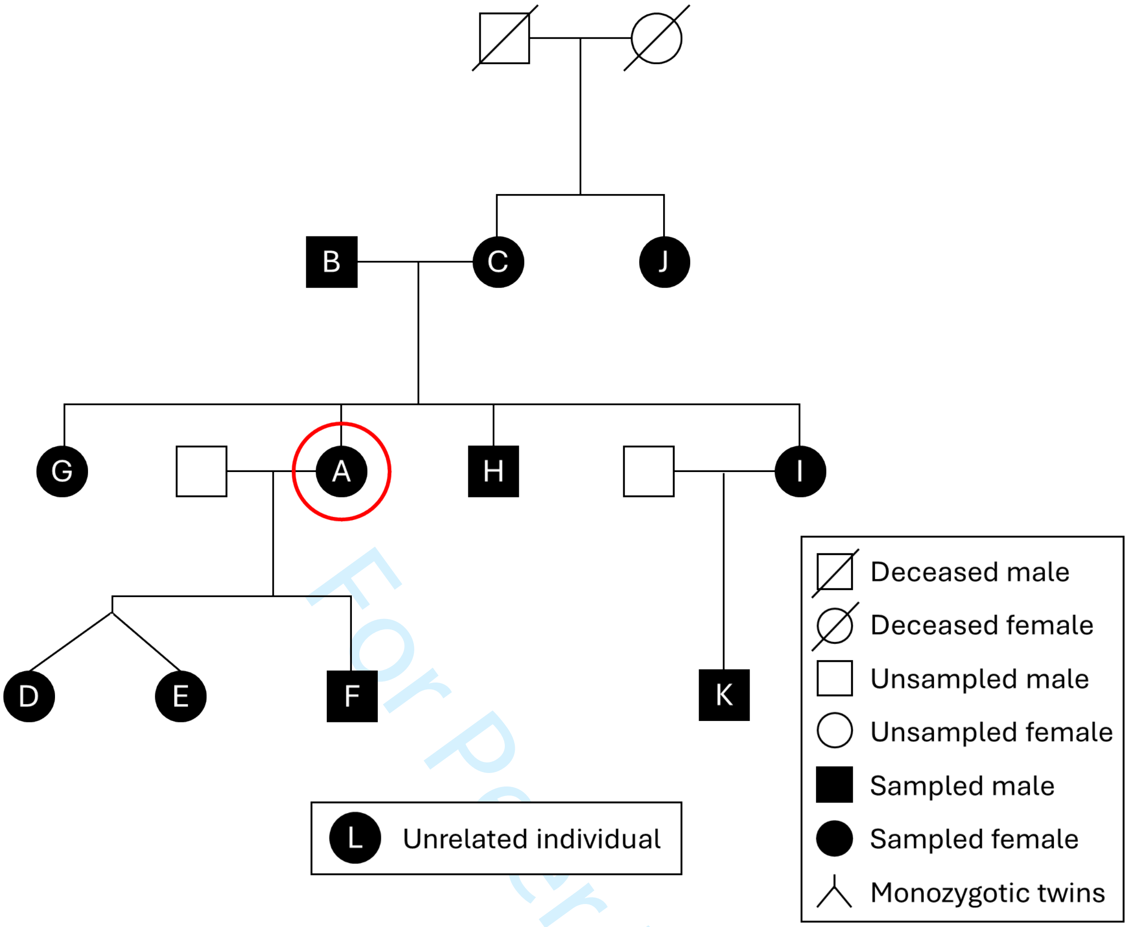

Figure 2. Pedigree Group 2, with letters corresponding to Individuals A through L.[14] Individuals included in the study are filled in (black), with living relatives linking the family members not filled (white). Deceased relatives are crossed out. Individual L is unrelated to all individuals in the group. The central individual (Individual A) is circled in red.

Table 2. Direct-to-consumer kits available for Individuals A through L in Group 2.[14]

Sample ID	AncestryDNA	FamilyTreeDNA	23andMe	Living DNA
Individual A	✓	✓	✓	✓
Individual B	✓	✓	✓	✓
Individual C	✓	✓	✓	✓
Individual D	✗	✓	✗	✗
Individual E	✓	✓	✗	✗
Individual F	✗	✓	✗	✗
Individual G	✓	✓	✗	✗
Individual H	✓	✓	✗	✗
Individual I	✓	✓	✗	✗
Individual J	✗	✓	✗	✗
Individual K	✗	✓	✗	✗
Individual L	✓	✗	✗	✗

Table 3. Call rate and autosomal heterozygosity for Individual 1 (Pedigree Group 1) and Individual A (Pedigree Group 2) for the full Kintelligence profile, profiles generated with locus dropout ranging from 5 to 30% and profiles generated with allele dropout ranging from 5 to 30%.

Profile	**Individual 1**		**Individual A**	
	Call Rate (%)	**Autosomal Heterozygosity (%)**	**Call Rate (%)**	**Autosomal Heterozygosity (%)**
Full profile	99.85	48.04	99.41	47.51
5% locus dropout	95.00	48.19	95.00	47.52
10% locus dropout	90.00	48.26	90.00	47.94
15% locus dropout	85.00	48.55	85.00	47.90
20% locus dropout	80.00	48.28	80.00	47.68
25% locus dropout	75.00	48.36	75.00	47.56
30% locus dropout	70.00	48.47	70.00	47.42
5% allele dropout	99.85	45.64	99.41	45.14
10% allele dropout	99.85	43.24	99.41	42.77
15% allele dropout	99.85	40.84	99.41	40.39
20% allele dropout	99.85	38.44	99.41	38.02
25% allele dropout	99.85	36.03	99.41	35.63
30% allele dropout	99.85	33.64	99.41	33.26

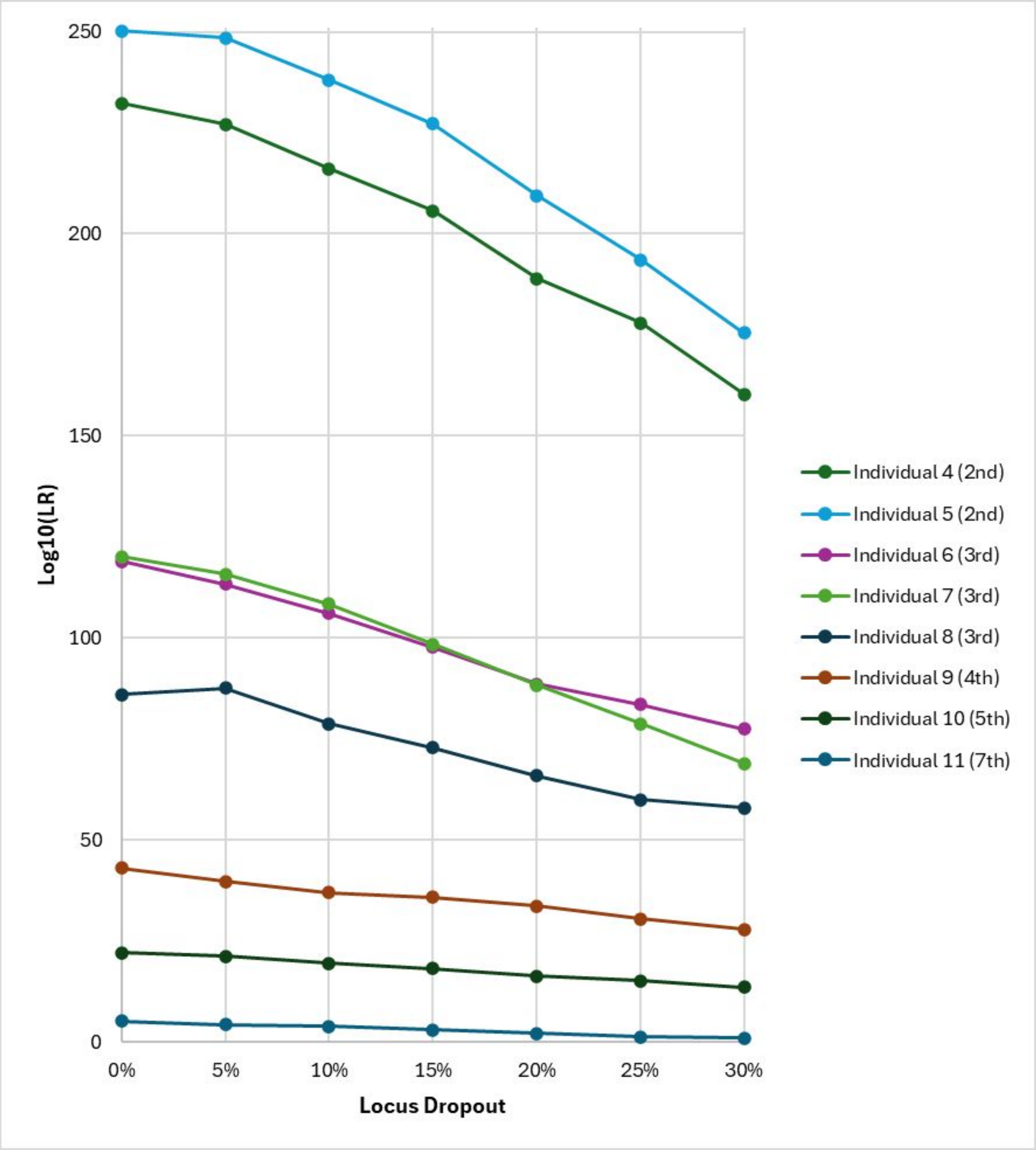

Figure 3. Log$_{10}$ LRs generated with locus dropout of Individual 1 ranging from 0 to 30% for all true relationships in Pedigree Group 1. The H_1 proposition was that the pair were related according to the true relationship degree. The H_2 proposition was that the pair were unrelated. The parent/offspring (Individual 2) was not plotted ($\log_{10}$ LR = $-\infty$). The full sibling (Individual 3) has not been plotted ($\log_{10}$ LR = ∞). 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative.

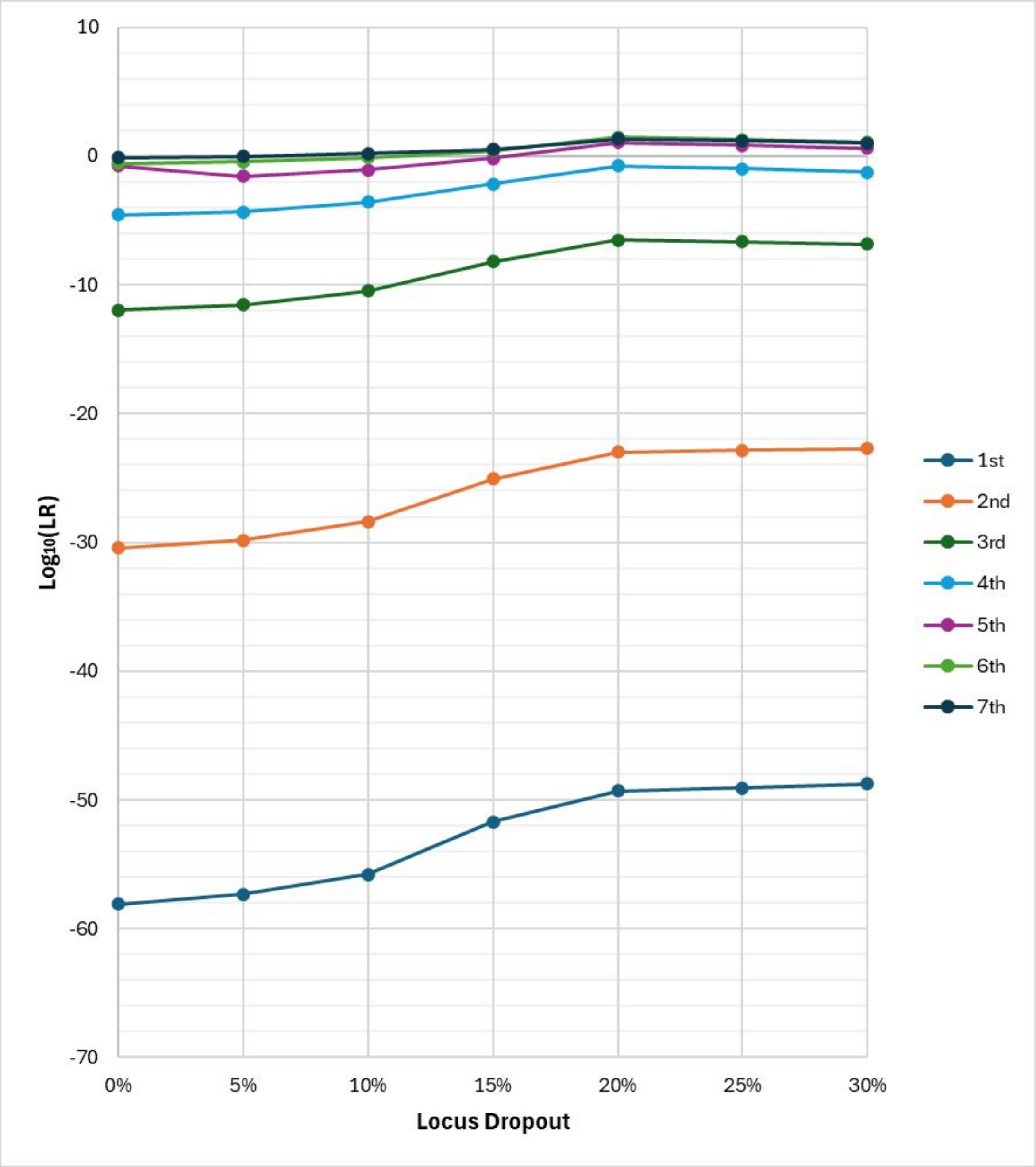

Figure 4. Log_{10} LRs generated with locus dropout of Individual 1 ranging from 0 to 30% and a true unrelated individual (Individual 12). The H_1 proposition was that the pair were related according to a specific relationship degree. The H_2 proposition was that the pair were unrelated (true). Parent/offspring tests have not been included (log_{10} LR = -∞). 1st: first degree relative; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 6th: sixth degree relative; 7th: seventh degree relative.

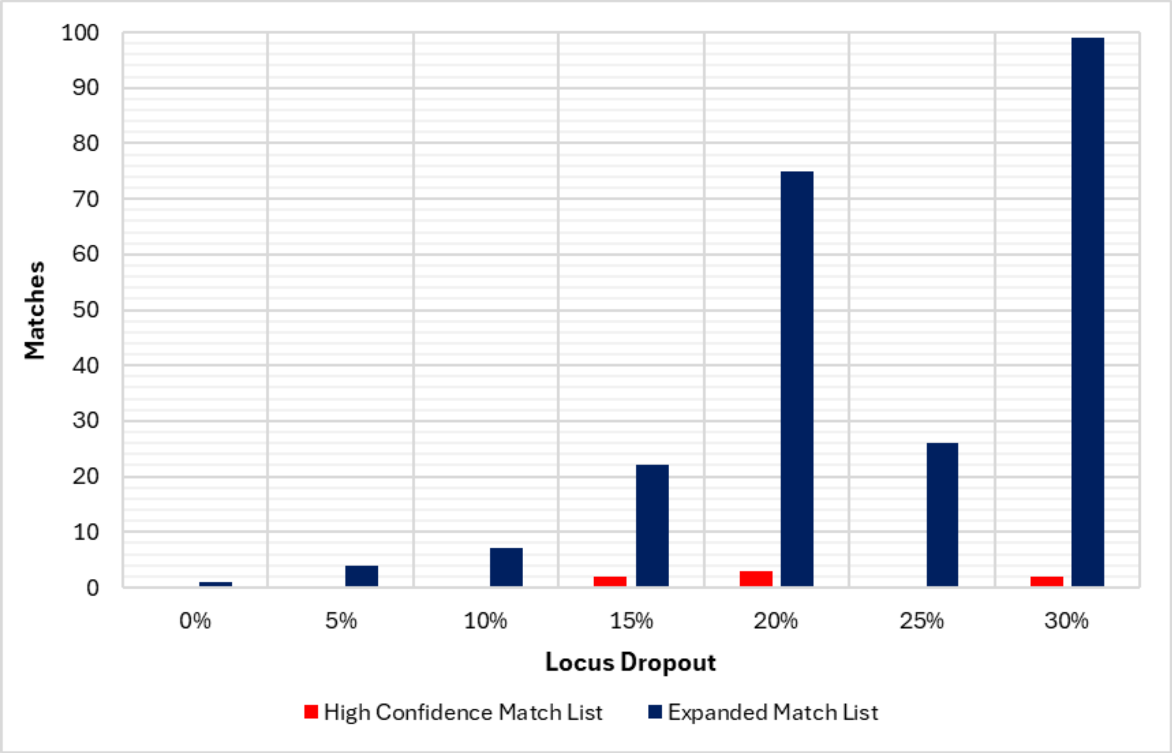

Figure 5. Additional matches included in the high confidence and expanded match lists on GEDmatch PRO™ that were not known genetic relatives of Individual 1 at various degrees of locus dropout.

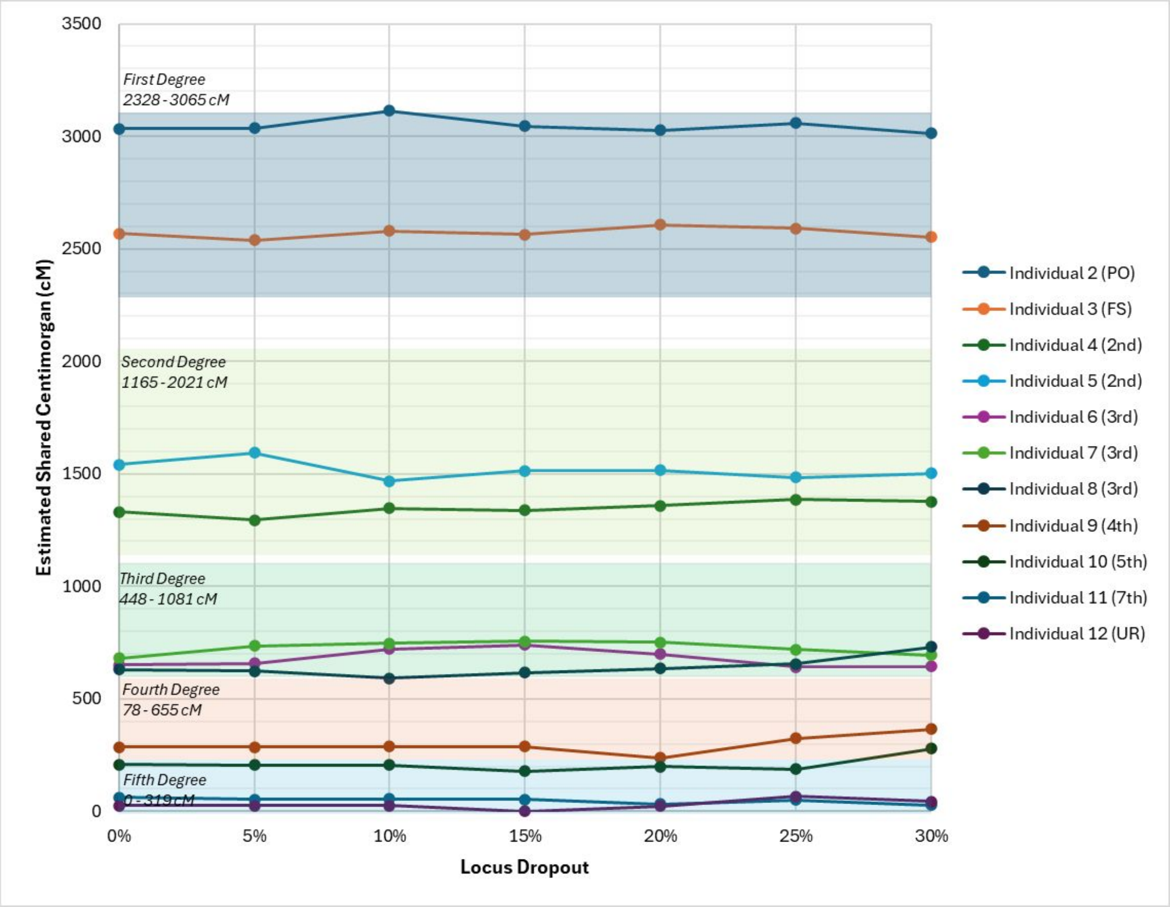

Figure 6. Estimated shared centimorgan (cM) values shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with locus dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12] PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

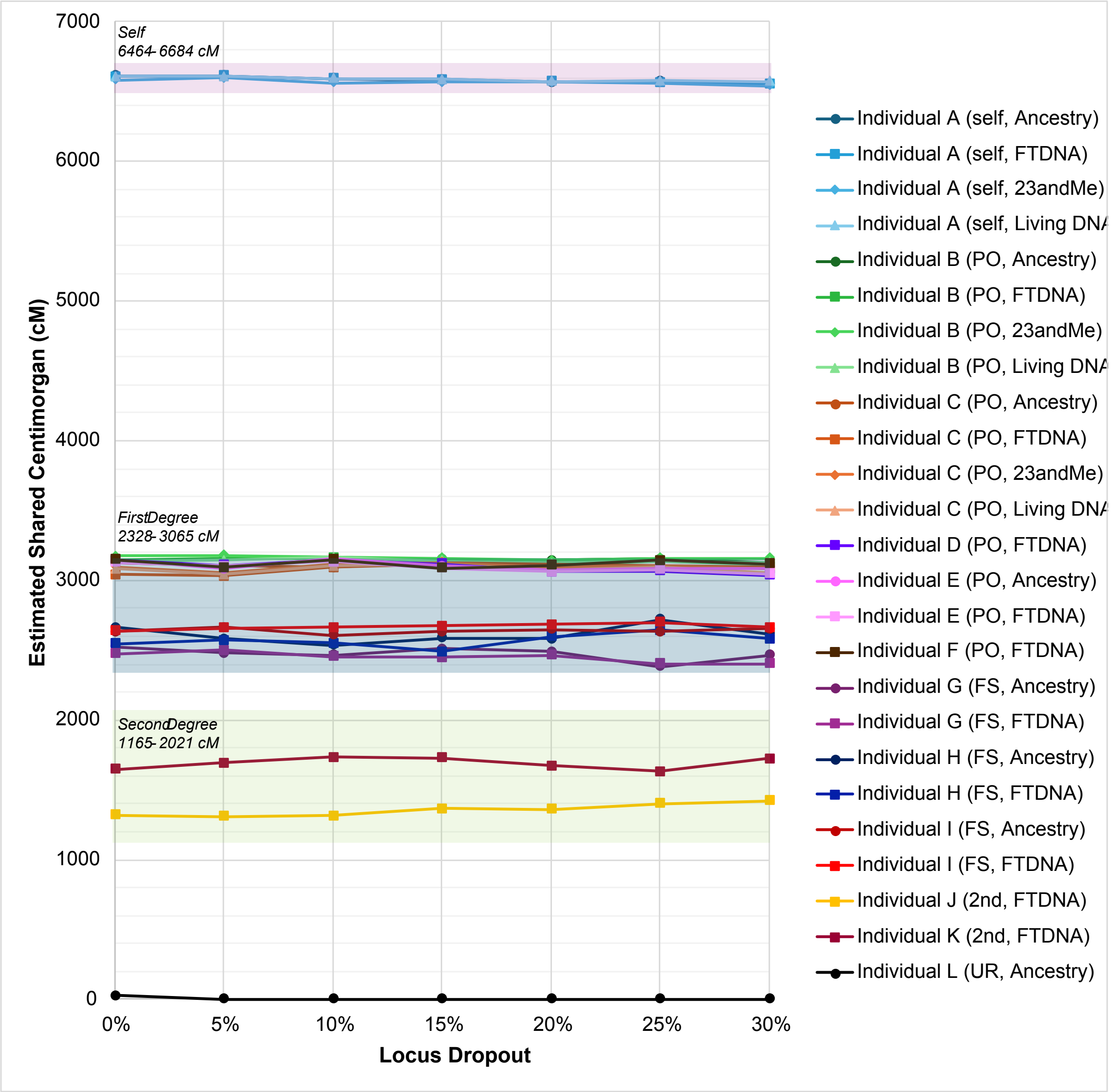

Figure 7. Estimated shared centimorgan (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with locus dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12] *PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.*

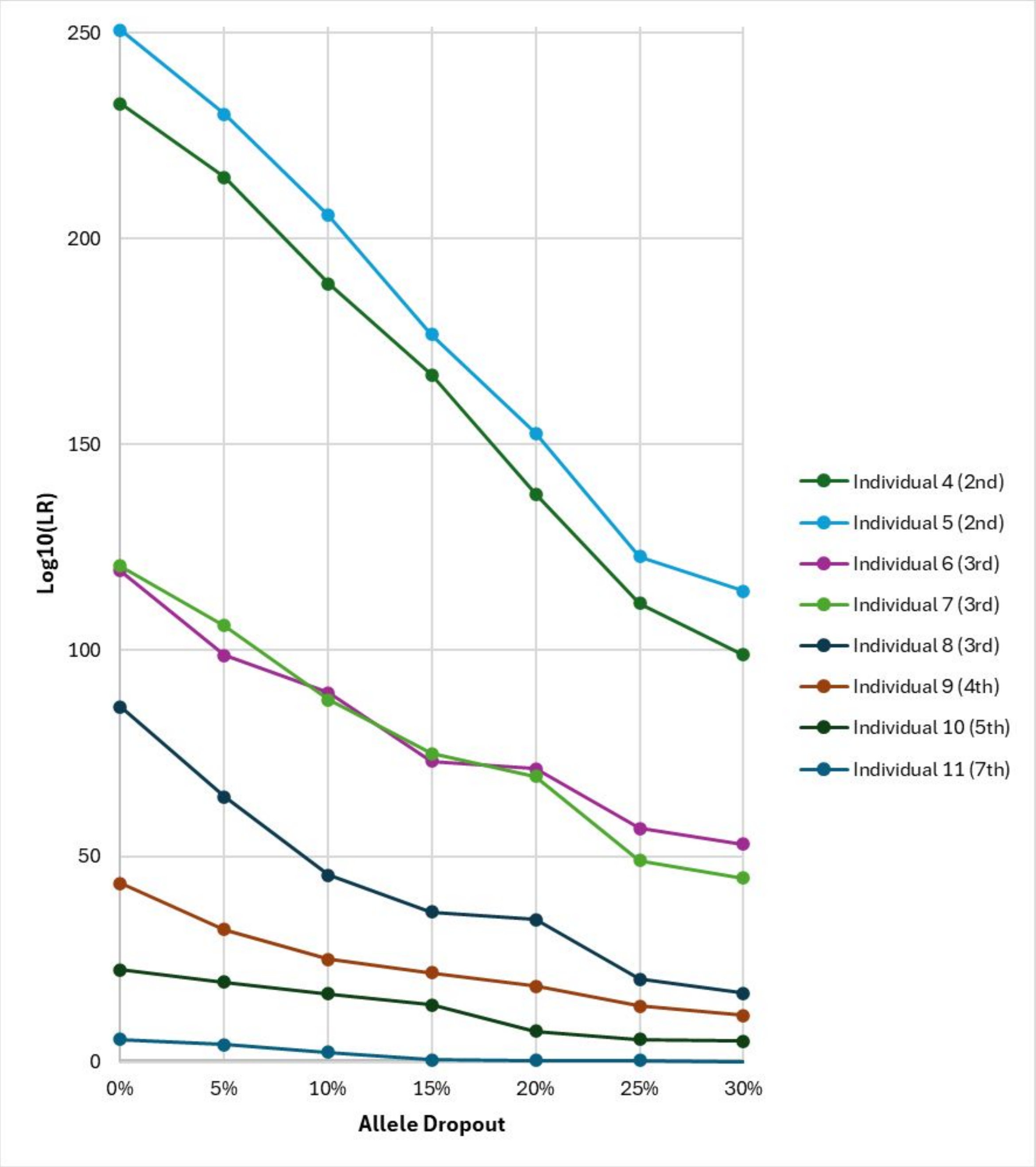

Figure 8. Log$_{10}$ LRs generated with allele dropout of Individual 1 ranging from 0 to 30% for all true relationships in Pedigree Group 1. The H_1 proposition was that the pair were related according to the true relationship degree. The H_2 proposition was that the pair were unrelated. The parent/offspring was not plotted ($\log_{10}$ LR = -∞). The full sibling has not been plotted ($\log_{10}$ LR = ∞). 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative.

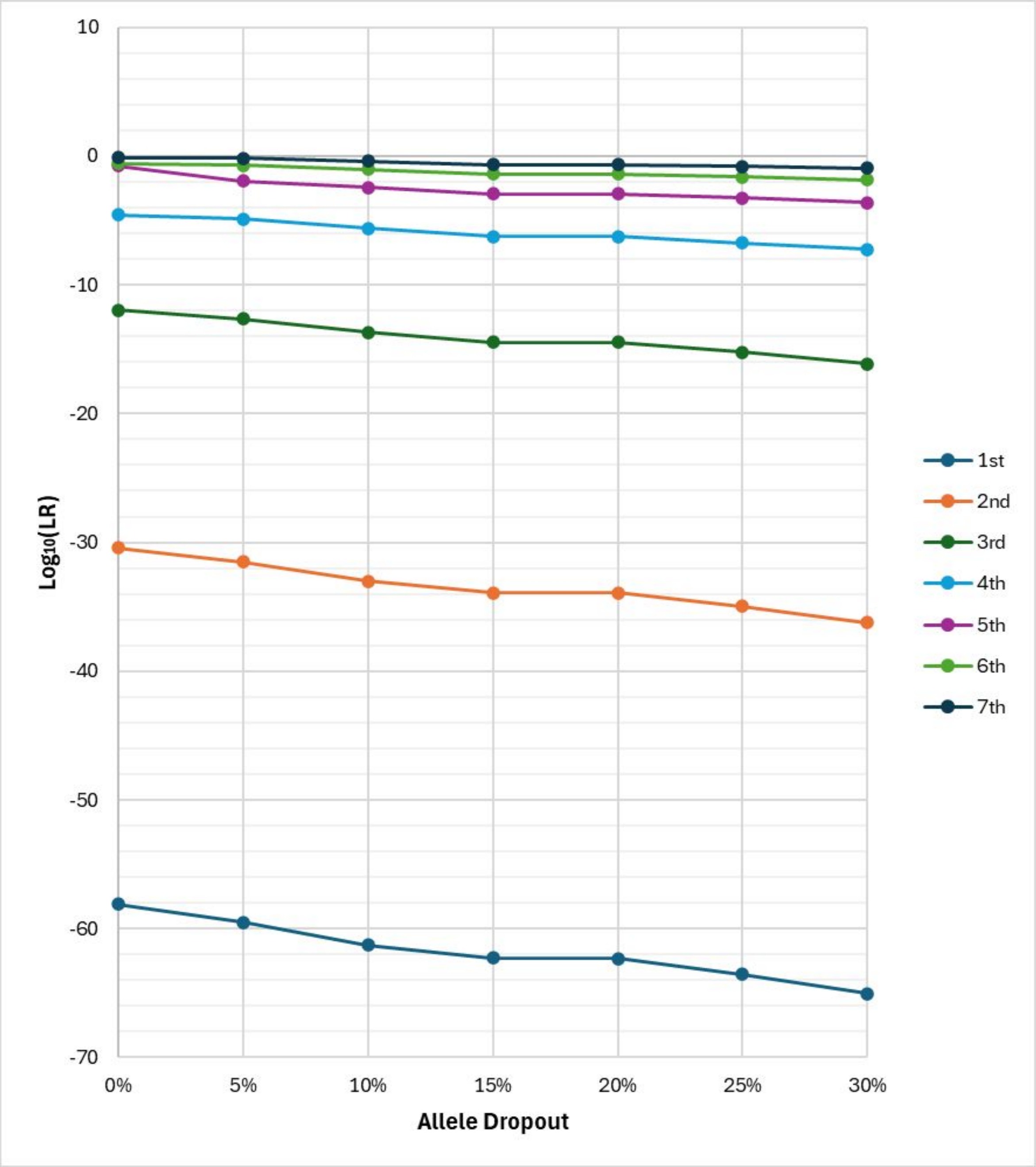

Figure 9. Log$_{10}$ LRs generated with allele dropout of Individual 1 ranging from 0 to 30% and a true unrelated individual (Individual 12). The H_1 proposition was that the pair were related according to a specific relationship degree. The H_2 proposition was that the pair were unrelated (true). Parent/offspring tests have not been included as ($\log_{10}$ LR = -∞). 1st: first degree relative; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 6th: sixth degree relative; 7th: seventh degree relative.

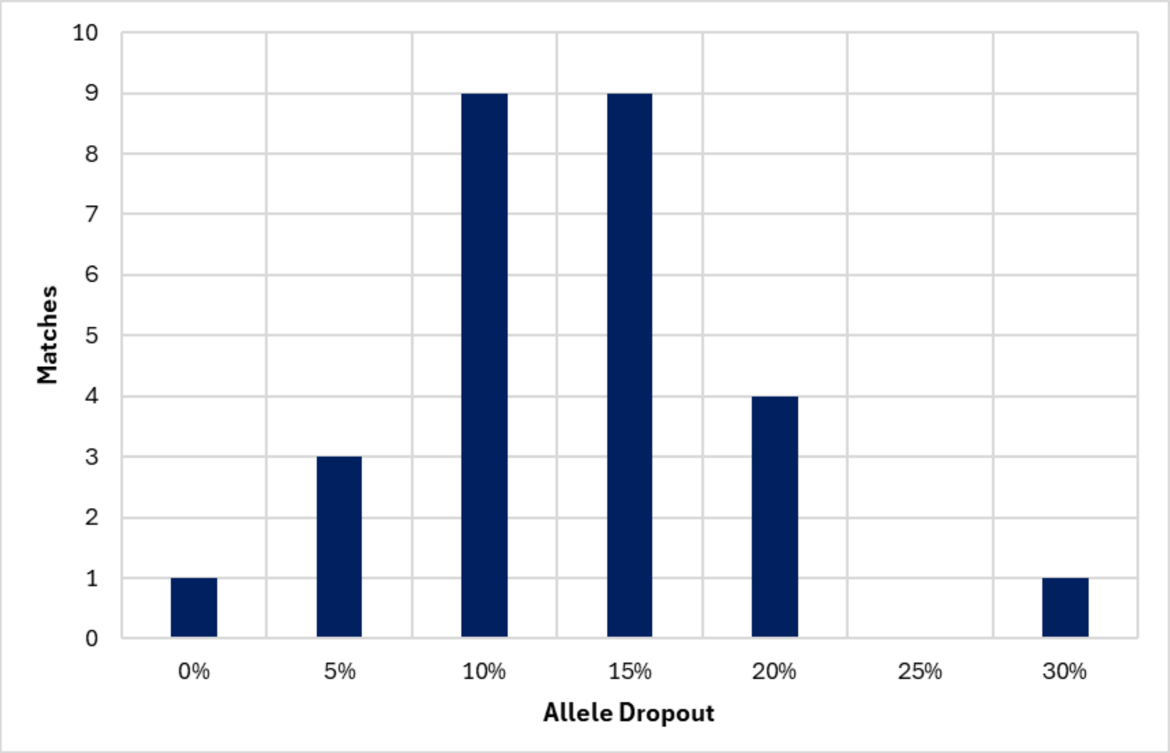

Figure 10. Additional matches included in the expanded match list on GEDmatch PRO™ that were not known genetic relatives of Individual 1 at various degrees of allele dropout.

Table 4. Estimated shared centimorgan (cM) results between the Individual 1 Kintelligence profiles with allele dropout ranging from 0 to 30%.

Allele Dropout	0%	5%	10%	15%	20%	25%	30%
0%		6631.3	5061.6	3490.7	3341.5	3341.5	3341.5
5%	6631.3		6661.7	5194.3	3493.7	3341.5	3341.5
10%	5061.6	6661.7		6681.4	5024.3	3493.5	3341.5
15%	3490.7	5194.3	6681.4		6683	5223.8	3598.5
20%	3341.5	3493.7	5024.3	6683		6683	4900.7
25%	3341.5	3341.5	3493.5	5223.8	6683		6683
30%	3341.5	3341.5	3341.5	3598.5	4900.7	6683	

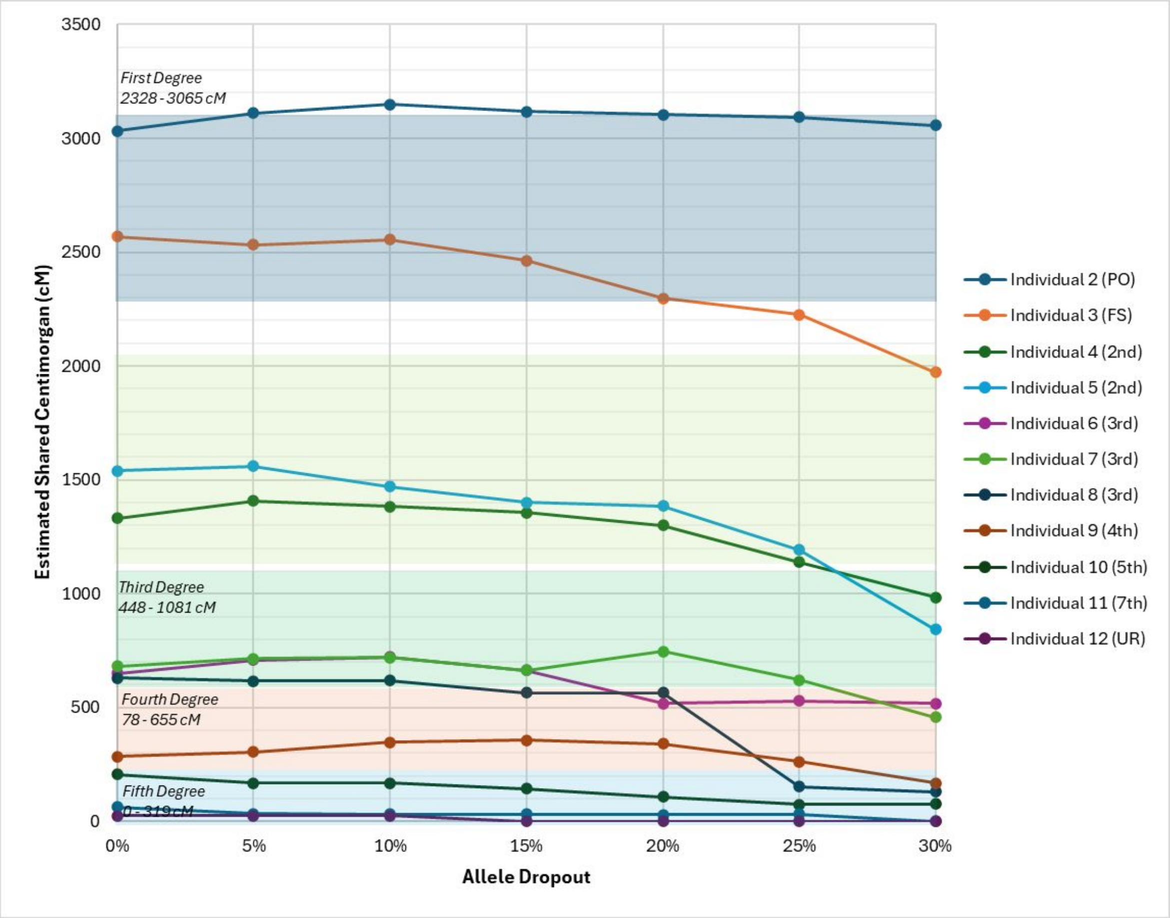

Figure 11. Estimated shared centimorgan (cM) values shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with allele dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12] *PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.*

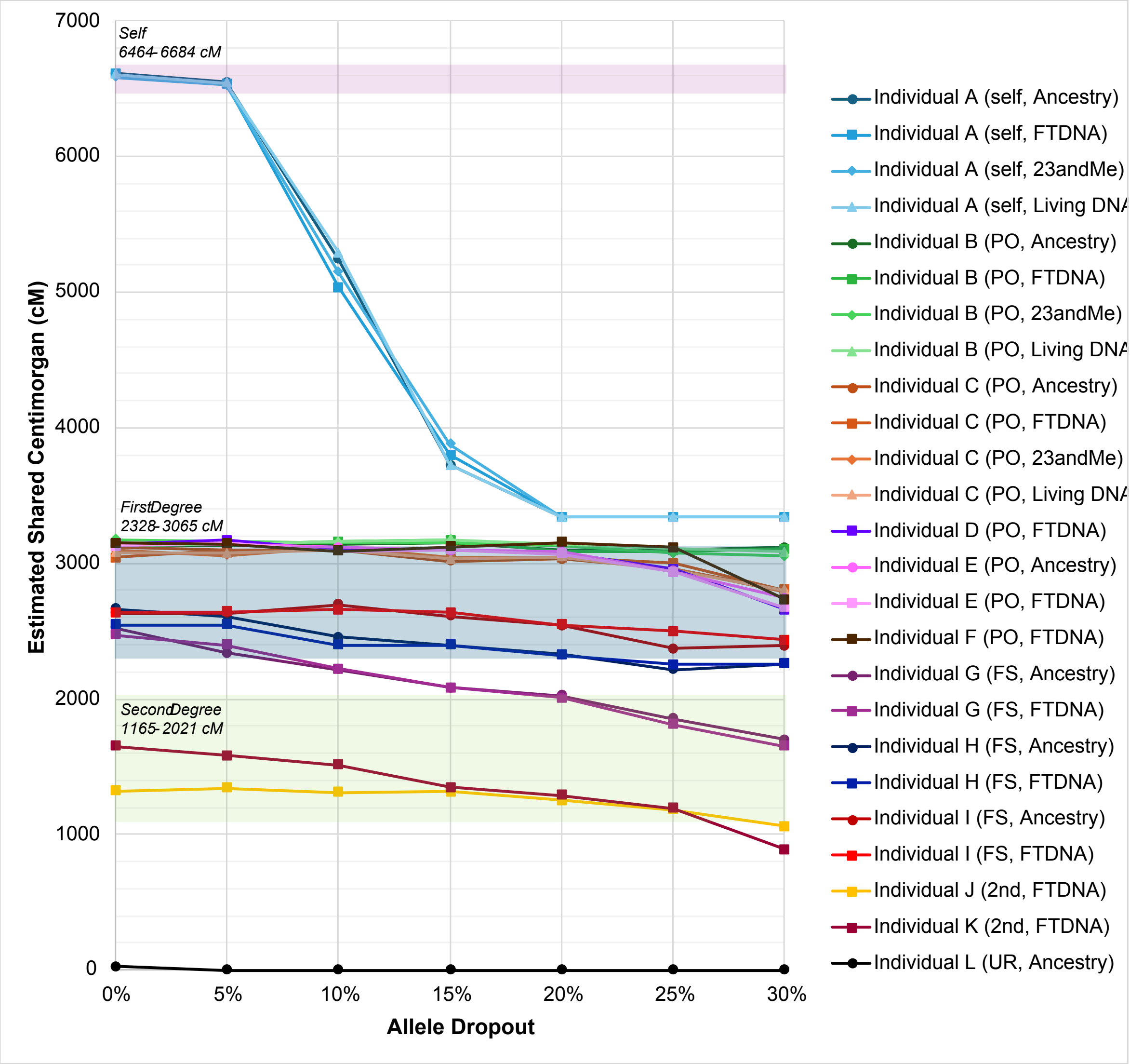

Figure 12. Estimated shared centimorgan (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with allele dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12] *PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.*

Supplementary Materials

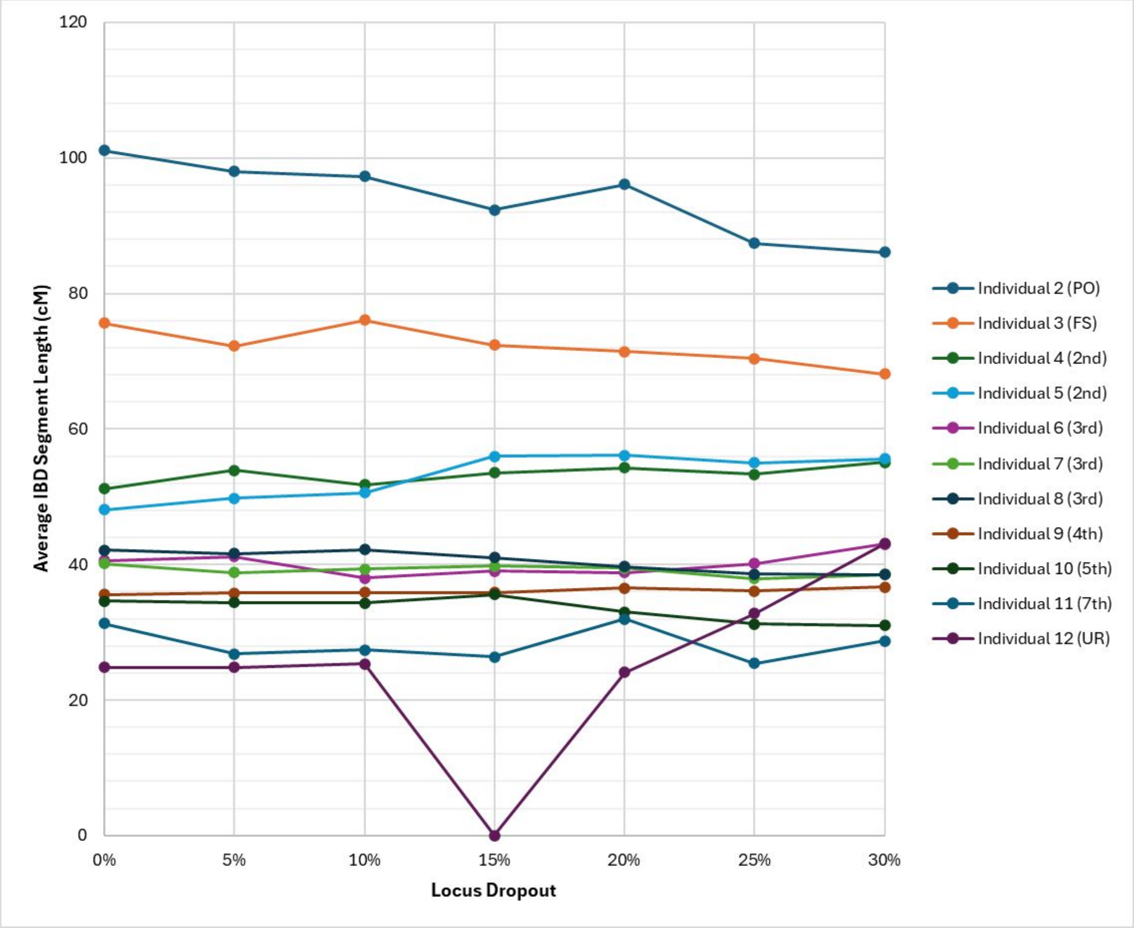

Figure S1. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with locus dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

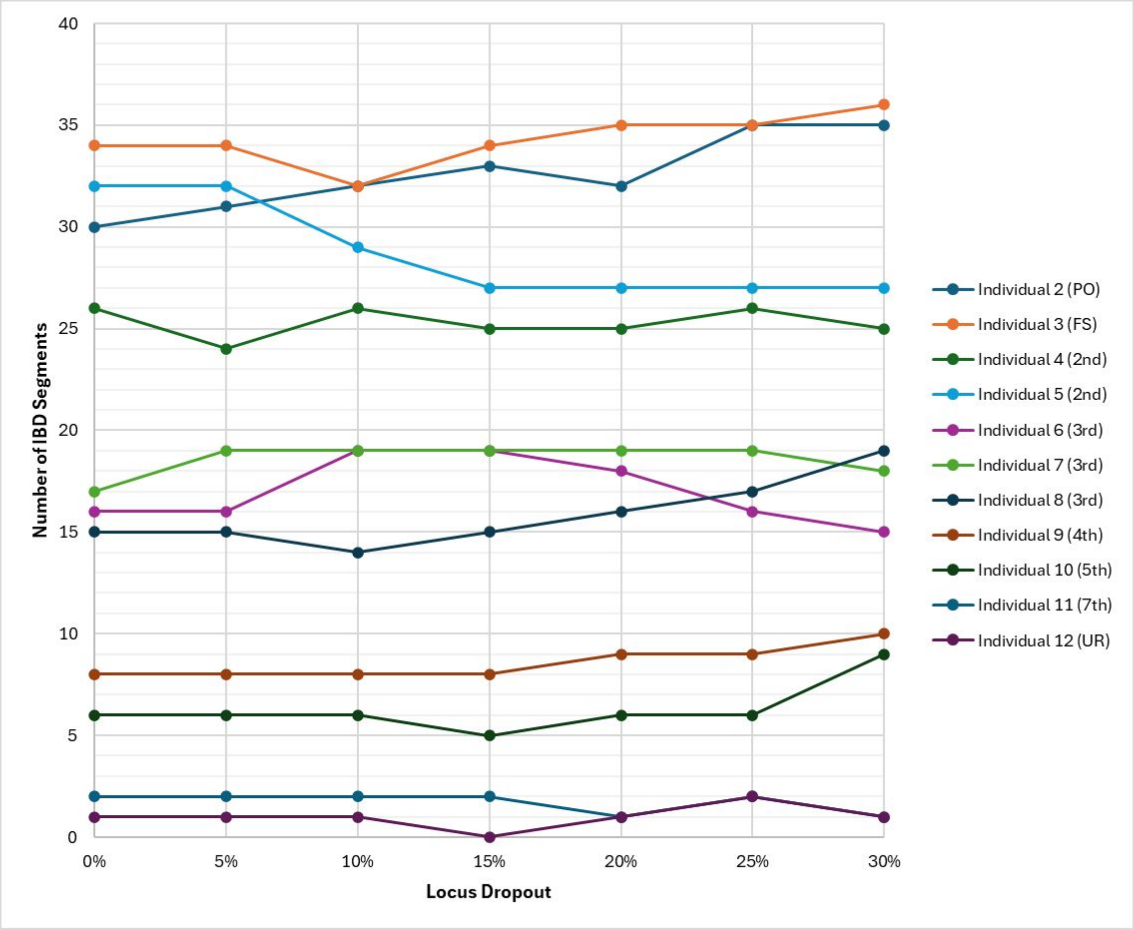

Figure S2. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with locus dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

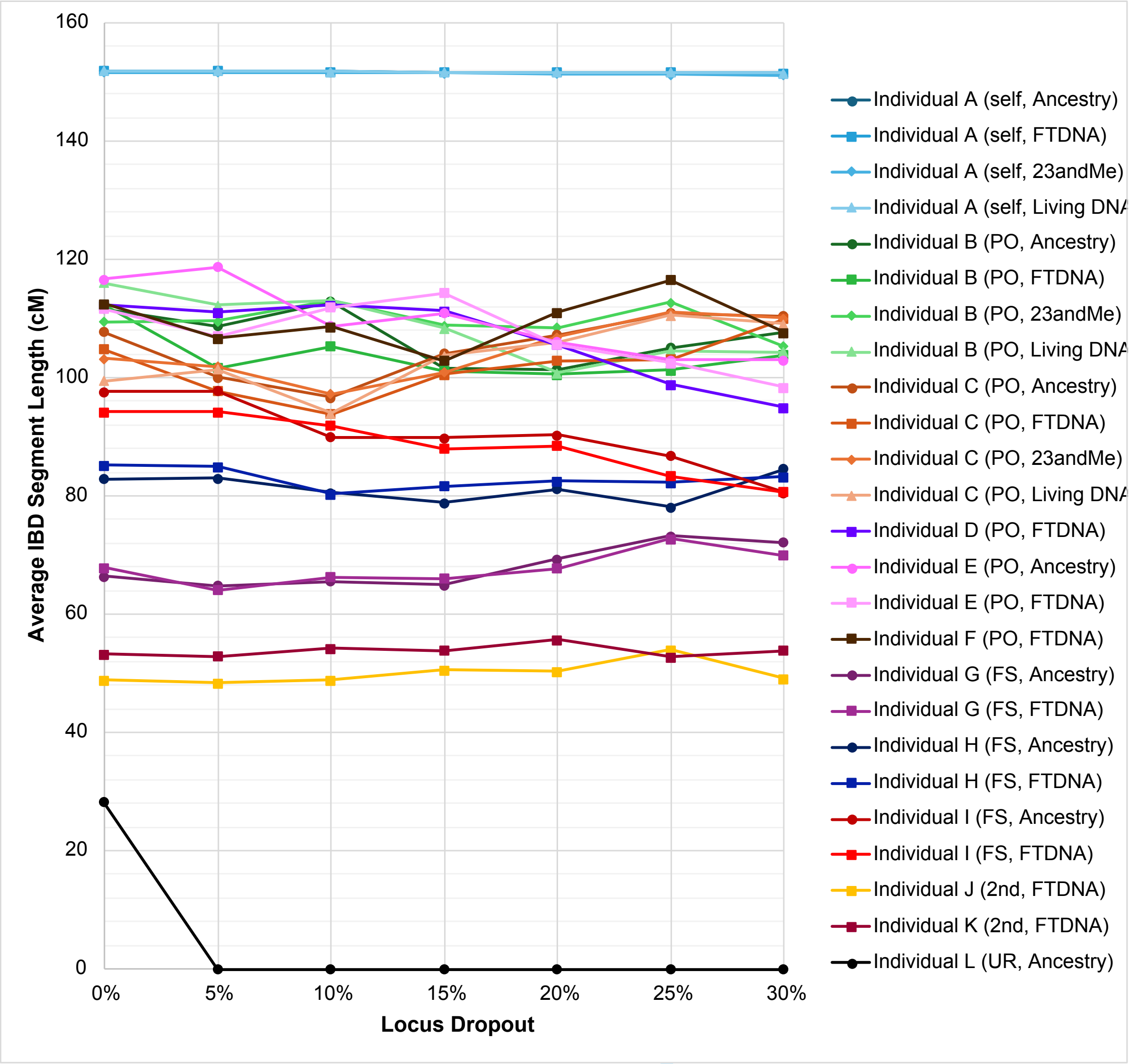

Figure S3. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with locus dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

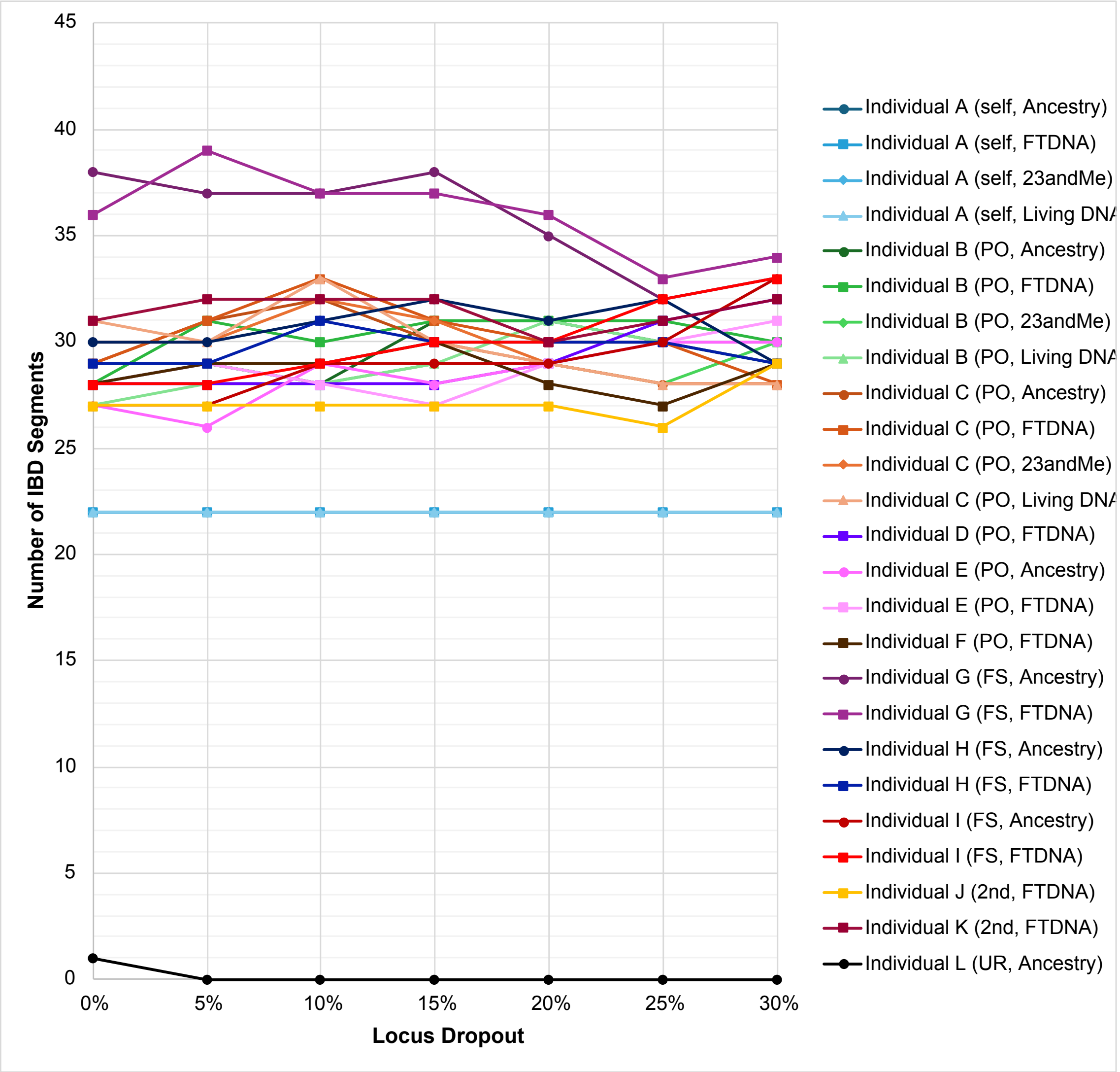

Figure S4. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with locus dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

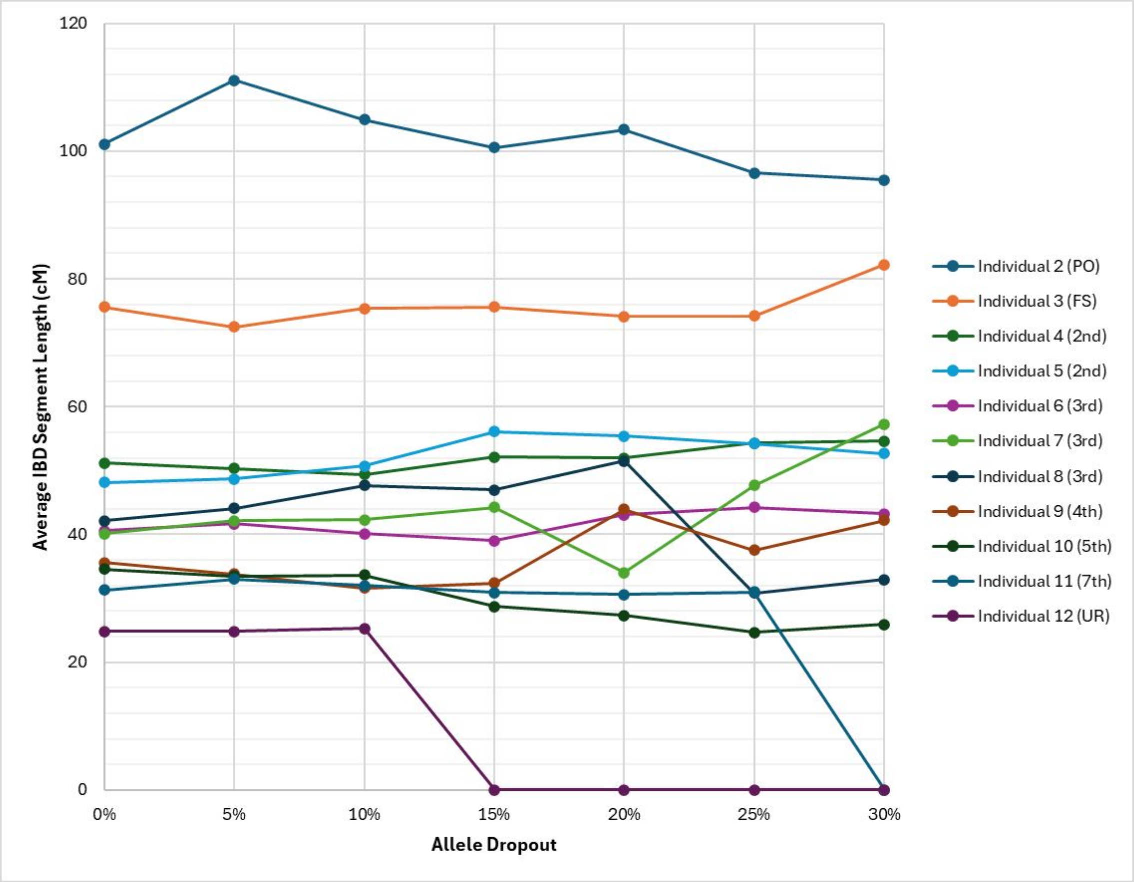

Figure S5. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with allele dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

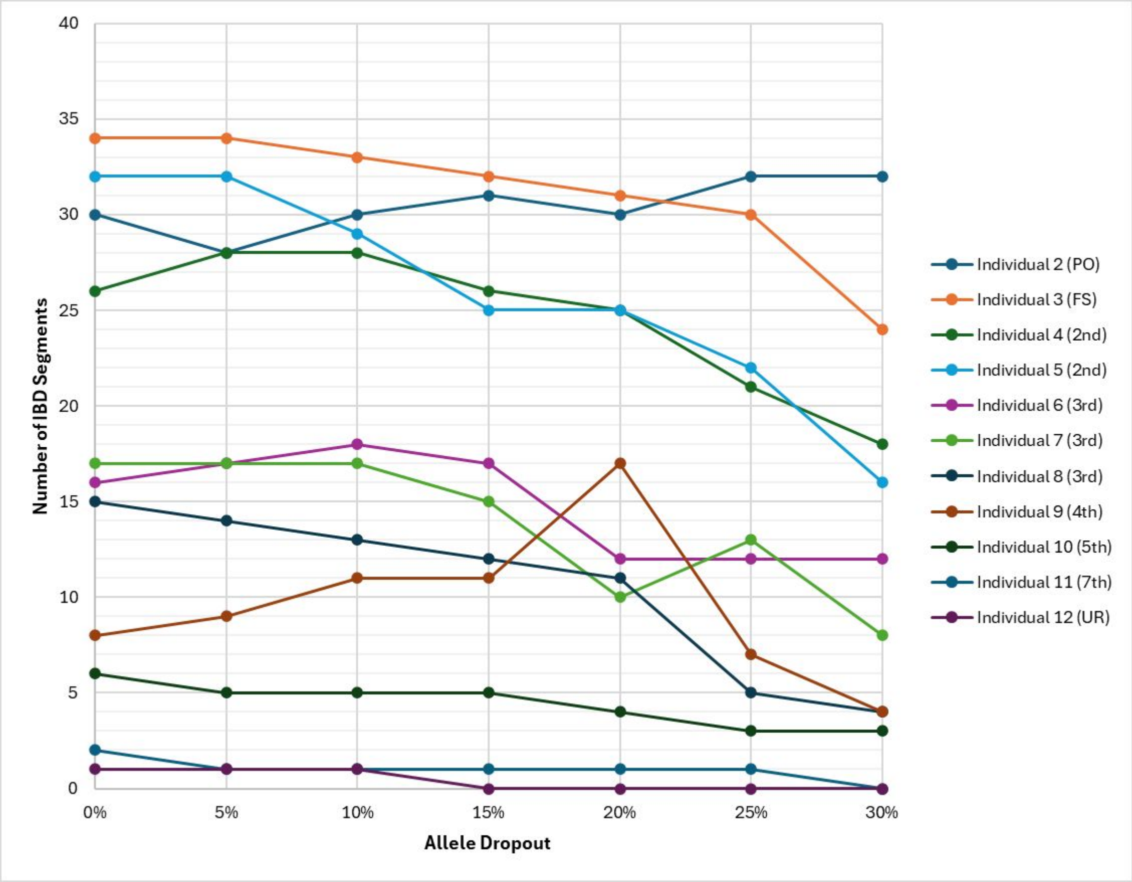

Figure S6. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with allele dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

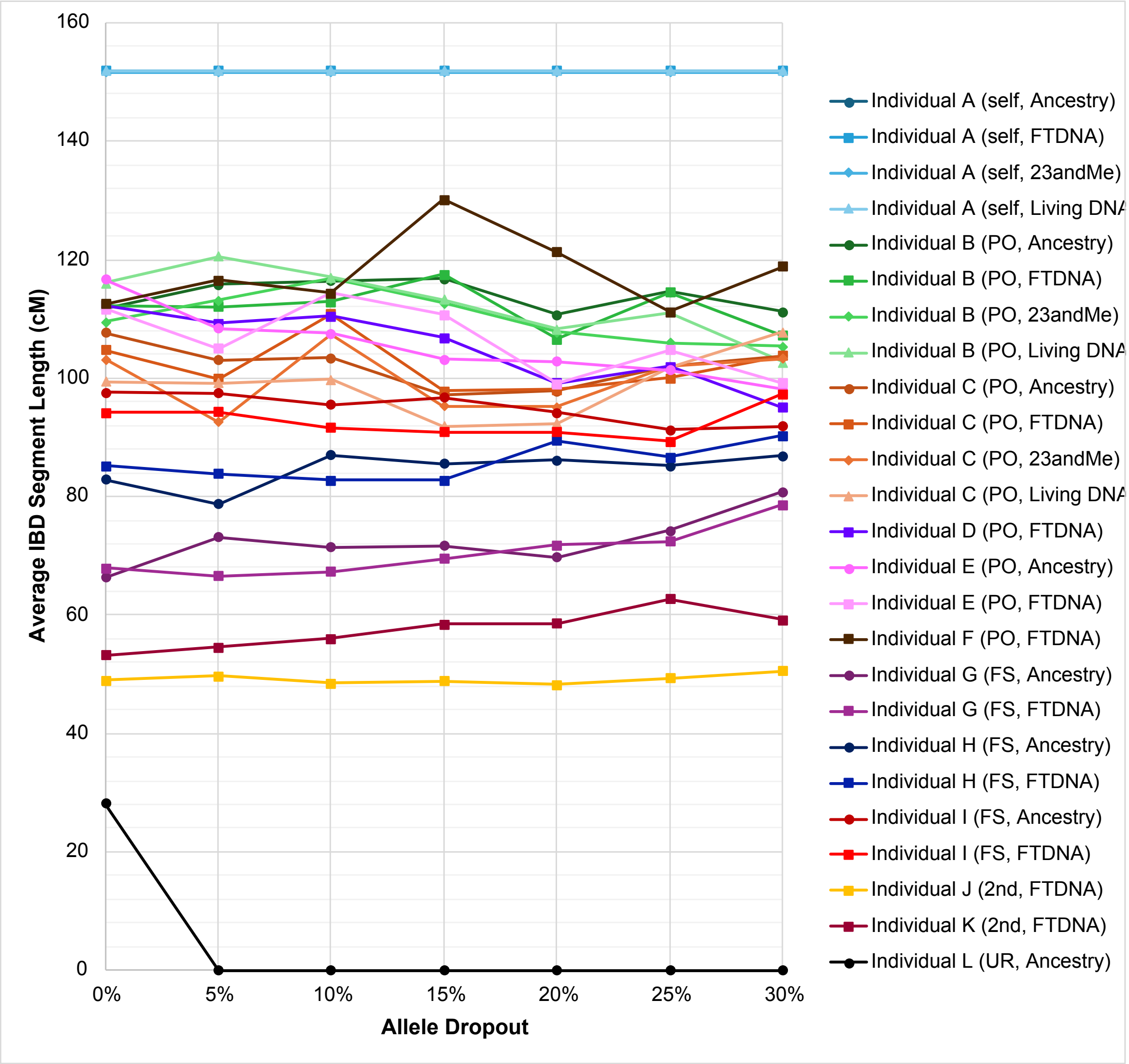

Figure S7. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with allele dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

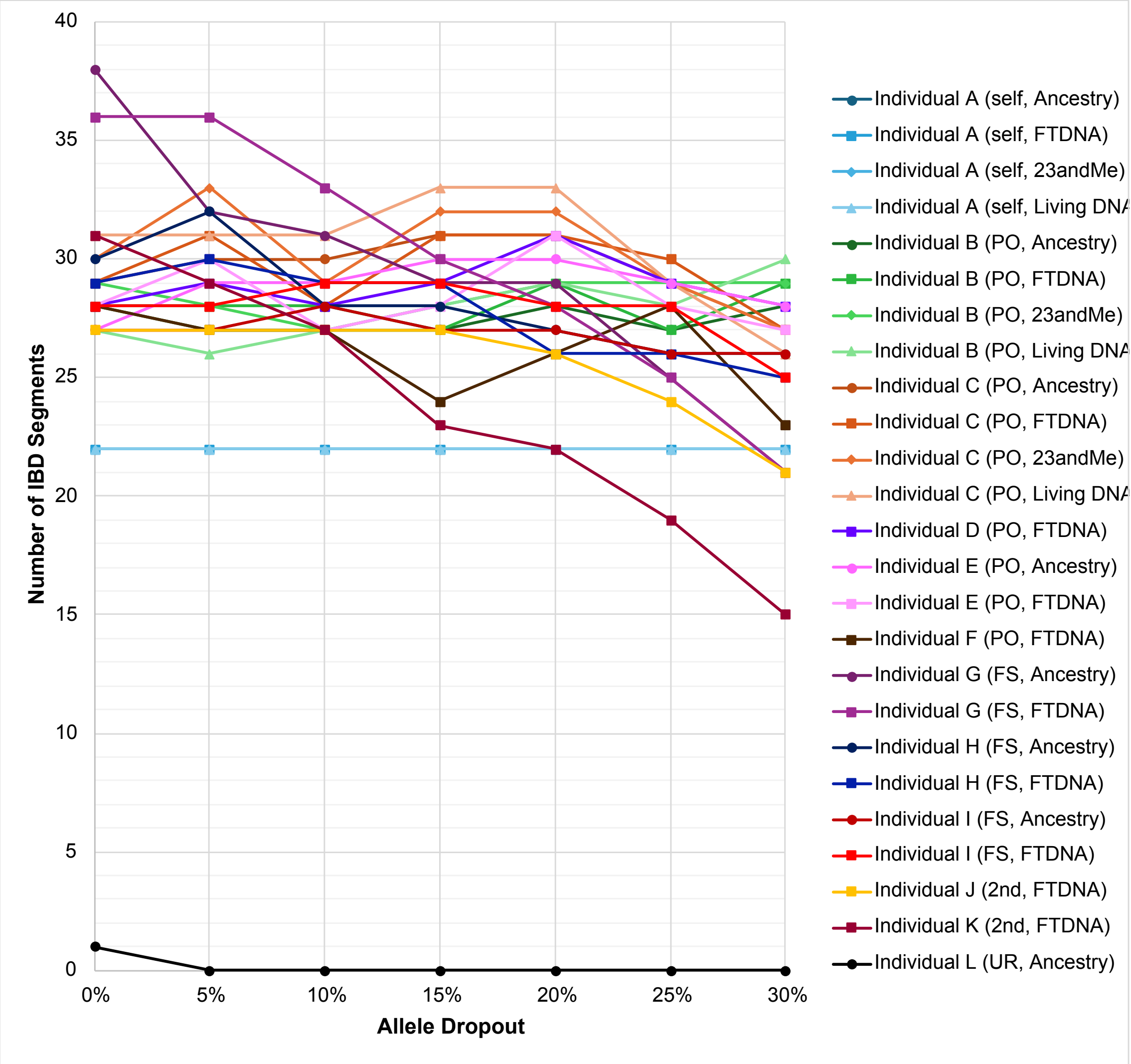

Figure S8. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with allele dropout ranging from 0 to 30%. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

Table 1. Verbal scale for log$_{10}$ LR results and the statistical support for each hypothesis.[15]

Log$_{10}$ LR	Interpretation
≤ –5	Very strong statistical support for H_2
–4	Strong statistical support for H_2
–3	Moderately strong statistical support for H_2
–2	Moderate statistical support for H_2
–1	Limited statistical support for H_2
0	Uninformative
1	Limited statistical support for H_1
2	Moderate statistical support for H_1
3	Moderately strong statistical support for H_1
4	Strong statistical support for H_1
≥ 5	Very strong statistical support for H_1

Table 2. Direct-to-consumer kits available for Individuals A through L in Group 2.[14]

Sample ID	AncestryDNA	FamilyTreeDNA	23andMe	Living DNA
Individual A	✓	✓	✓	✓
Individual B	✓	✓	✓	✓
Individual C	✓	✓	✓	✓
Individual D	✗	✓	✗	✗
Individual E	✓	✓	✗	✗
Individual F	✗	✓	✗	✗
Individual G	✓	✓	✗	✗
Individual H	✓	✓	✗	✗
Individual I	✓	✓	✗	✗
Individual J	✗	✓	✗	✗
Individual K	✗	✓	✗	✗
Individual L	✓	✗	✗	✗

Table 3. Call rate and autosomal heterozygosity for Individual 1 (Pedigree Group 1) and Individual A (Pedigree Group 2) for the full Kintelligence profile, profiles generated with locus dropout ranging from 5 to 30% and profiles generated with allele dropout ranging from 5 to 30%.

Profile	Individual 1		Individual A	
	Call Rate (%)	Autosomal Heterozygosity (%)	Call Rate (%)	Autosomal Heterozygosity (%)
Full profile	99.85	48.04	99.41	47.51
5% locus dropout	95.00	48.19	95.00	47.52

10% locus dropout	90.00	48.26	90.00	47.94
15% locus dropout	85.00	48.55	85.00	47.90
20% locus dropout	80.00	48.28	80.00	47.68
25% locus dropout	75.00	48.36	75.00	47.56
30% locus dropout	70.00	48.47	70.00	47.42
5% allele dropout	99.85	45.64	99.41	45.14
10% allele dropout	99.85	43.24	99.41	42.77
15% allele dropout	99.85	40.84	99.41	40.39
20% allele dropout	99.85	38.44	99.41	38.02
25% allele dropout	99.85	36.03	99.41	35.63
30% allele dropout	99.85	33.64	99.41	33.26

Table 4. Estimated shared centimorgan (cM) results between the Individual 1 Kintelligence profiles with allele dropout ranging from 0 to 30%.

Allele Dropout	0%	5%	10%	15%	20%	25%	30%
0%		6631.3	5061.6	3490.7	3341.5	3341.5	3341.5
5%	6631.3		6661.7	5194.3	3493.7	3341.5	3341.5
10%	5061.6	6661.7		6681.4	5024.3	3493.5	3341.5
15%	3490.7	5194.3	6681.4		6683	5223.8	3598.5
20%	3341.5	3493.7	5024.3	6683		6683	4900.7
25%	3341.5	3341.5	3493.5	5223.8	6683		6683
30%	3341.5	3341.5	3341.5	3598.5	4900.7	6683	

Figure 1. Pedigree Group 1, with numbers corresponding to Individuals 1 through 12.[14] Individuals included in the study are filled in (black), with living relatives linking the family members not filled (white). Deceased relatives are crossed out. Individual 12 is unrelated to all individuals in the group. The central individual (Individual 1) is circled in red.

Figure 2. Pedigree Group 2, with letters corresponding to Individuals A through L.[14] Individuals included in the study are filled in (black), with living relatives linking the family members not filled (white). Deceased relatives are crossed out. Individual L is unrelated to all individuals in the group. The central individual (Individual A) is circled in red.

Figure 3. Log_{10} LRs generated with locus dropout of Individual 1 ranging from 0 to 30% for all true relationships in Pedigree Group 1. The H_1 proposition was that the pair were related according to the true relationship degree. The H_2 proposition was that the pair were unrelated. The parent/offspring (Individual 2) was not plotted ($\log_{10}$ LR = $-\infty$). The full sibling (Individual 3) has not been plotted ($\log_{10}$ LR = ∞). 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative.

Figure 4. Log_{10} LRs generated with locus dropout of Individual 1 ranging from 0 to 30% and a true unrelated individual (Individual 12). The H_1 proposition was that the pair were related according to a specific relationship degree. The H_2 proposition was that the pair were unrelated (true). Parent/offspring tests have not been included ($\log_{10}$ LR = $-\infty$). 1st: first degree relative; 2nd: second degree relative; 3rd:

third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 6th: sixth degree relative; 7th: seventh degree relative.

Figure 5. Additional matches included in the high confidence and expanded match lists on GEDmatch PRO™ that were not known genetic relatives of Individual 1 at various degrees of locus dropout.

Figure 6. Estimated shared centimorgan (cM) values shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with locus dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12] PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

Figure 7. Estimated shared centimorgan (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with locus dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12] PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

Figure 8. Log_{10} LRs generated with allele dropout of Individual 1 ranging from 0 to 30% for all true relationships in Pedigree Group 1. The H_1 proposition was that the pair were related according to the true relationship degree. The H_2 proposition was that the pair were unrelated. The parent/offspring was not plotted ($\log_{10}$ LR = $-\infty$). The full sibling has not been plotted ($\log_{10}$ LR = ∞). 2nd: second degree

relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative.

Figure 9. Log_{10} LRs generated with allele dropout of Individual 1 ranging from 0 to 30% and a true unrelated individual (Individual 12). The H_1 proposition was that the pair were related according to a specific relationship degree. The H_2 proposition was that the pair were unrelated (true). Parent/offspring tests have not been included as ($\log_{10}$ LR = $-\infty$). 1st: first degree relative; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 6th: sixth degree relative; 7th: seventh degree relative.

Figure 10. Additional matches included in the expanded match list on GEDmatch PRO™ that were not known genetic relatives of Individual 1 at various degrees of allele dropout.

Figure 11. Estimated shared centimorgan (cM) values shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with allele dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12] PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

Figure 12. Estimated shared centimorgan (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with allele dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.[12]

PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

Figure S1. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual 1 with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

Figure S2. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual 1 with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

Figure S3. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual A with locus dropout ranging from 0 to 30% and the direct-to-consumer profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

Figure S4. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual A with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

Figure S5. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual 1 with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

Figure S6. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual 1 with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

Figure S7. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual A with allele dropout ranging from 0 to 30% and the direct-to-consumer profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

Figure S8. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual A with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

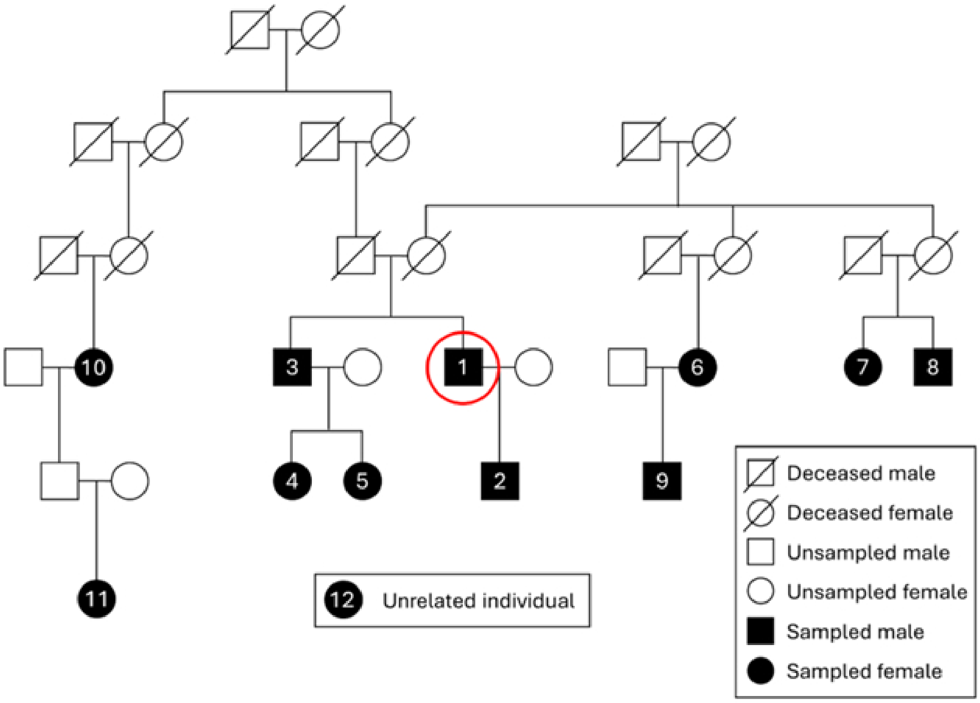

Figure 1. Pedigree Group 1, with numbers corresponding to Individuals 1 through 12.14 Individuals included in the study are filled in (black), with living relatives linking the family members not filled (white). Deceased relatives are crossed out. Individual 12 is unrelated to all individuals in the group. The central individual (Individual 1) is circled in red.

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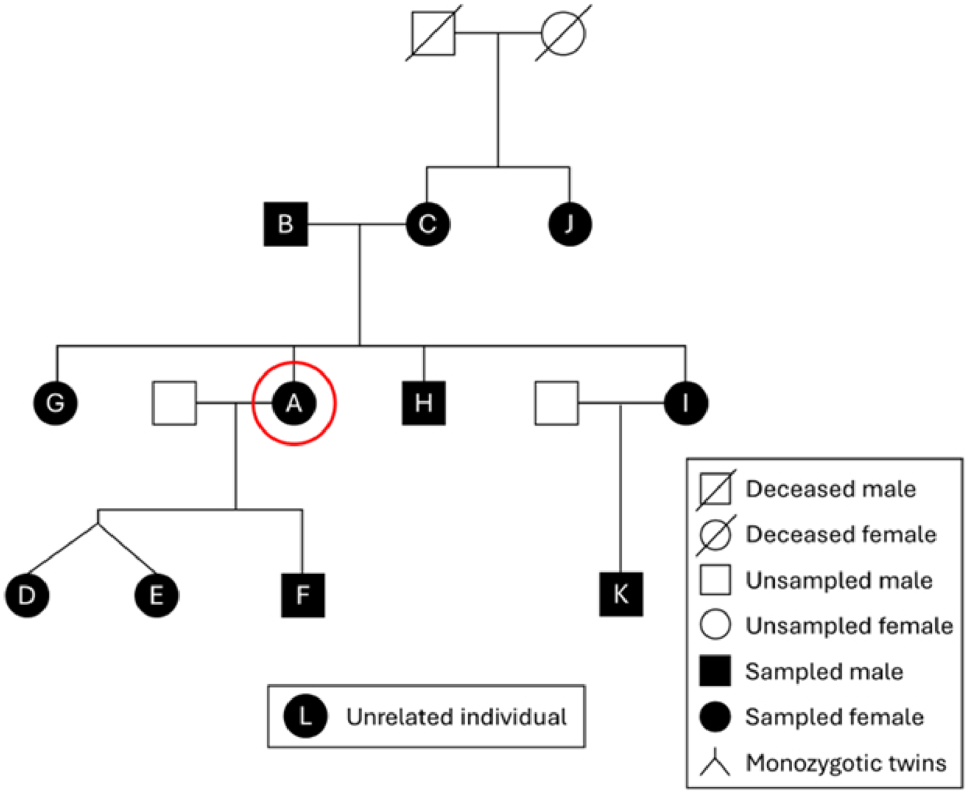

Figure 2. Pedigree Group 2, with letters corresponding to Individuals A through L.14 Individuals included in the study are filled in (black), with living relatives linking the family members not filled (white). Deceased relatives are crossed out. Individual L is unrelated to all individuals in the group. The central individual (Individual A) is circled in red.

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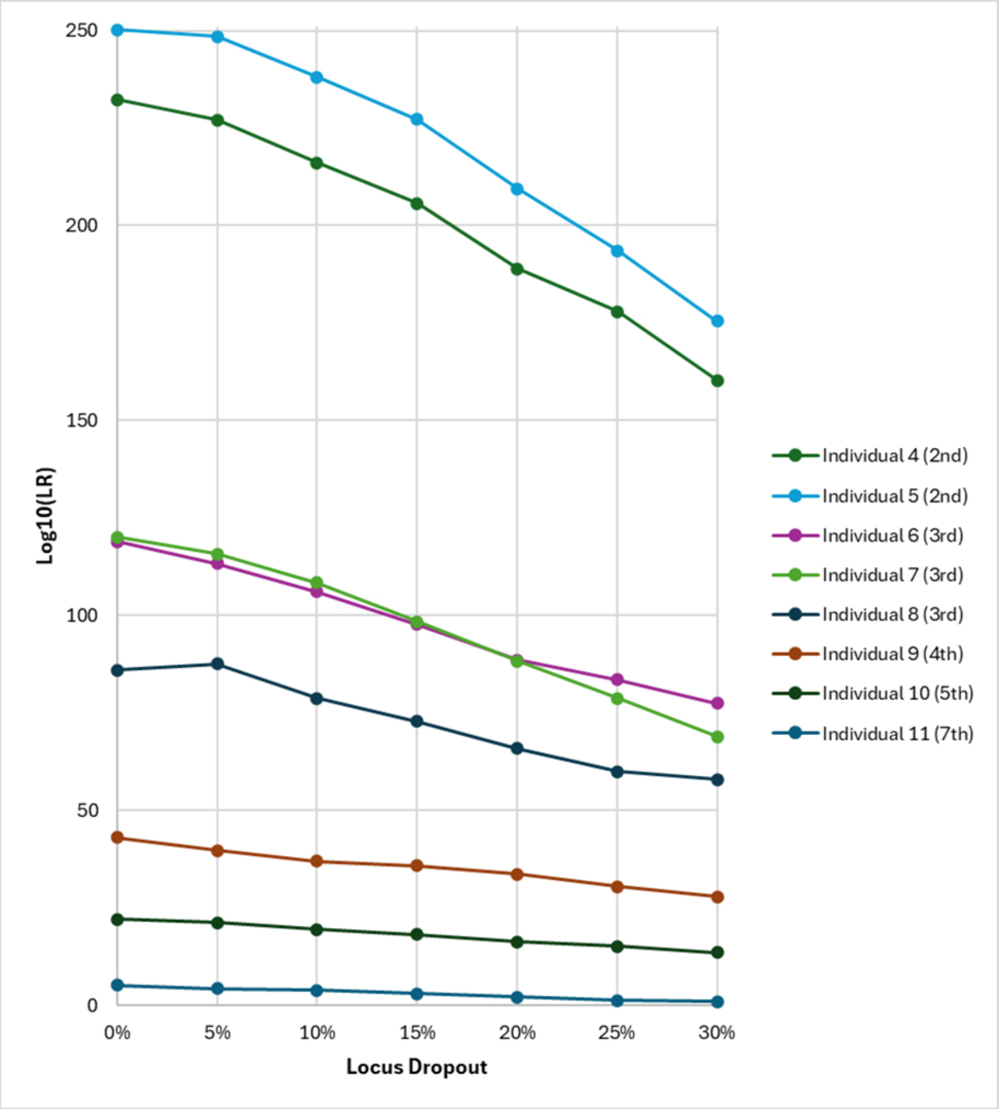

Figure 3. Log10 LRs generated with locus dropout of Individual 1 ranging from 0 to 30% for all true relationships in Pedigree Group 1. The H1 proposition was that the pair were related according to the true relationship degree. The H2 proposition was that the pair were unrelated. The parent/offspring (Individual 2) was not plotted (log10 LR = -∞). The full sibling (Individual 3) has not been plotted (log10 LR = ∞). 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative.

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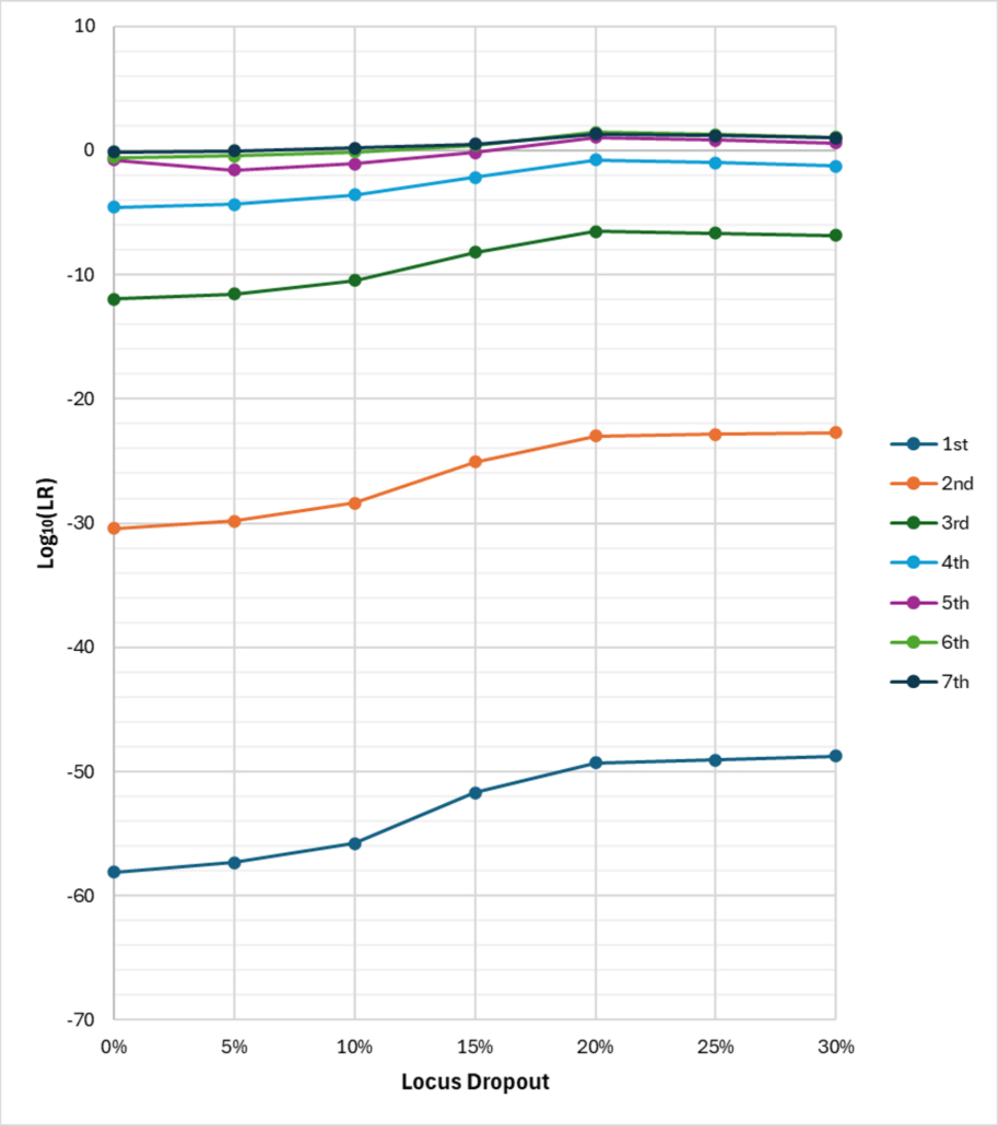

Figure 4. Log10 LRs generated with locus dropout of Individual 1 ranging from 0 to 30% and a true unrelated individual (Individual 12). The H1 proposition was that the pair were related according to a specific relationship degree. The H2 proposition was that the pair were unrelated (true). Parent/offspring tests have not been included (log10 LR = -∞). 1st: first degree relative; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 6th: sixth degree relative; 7th: seventh degree relative.

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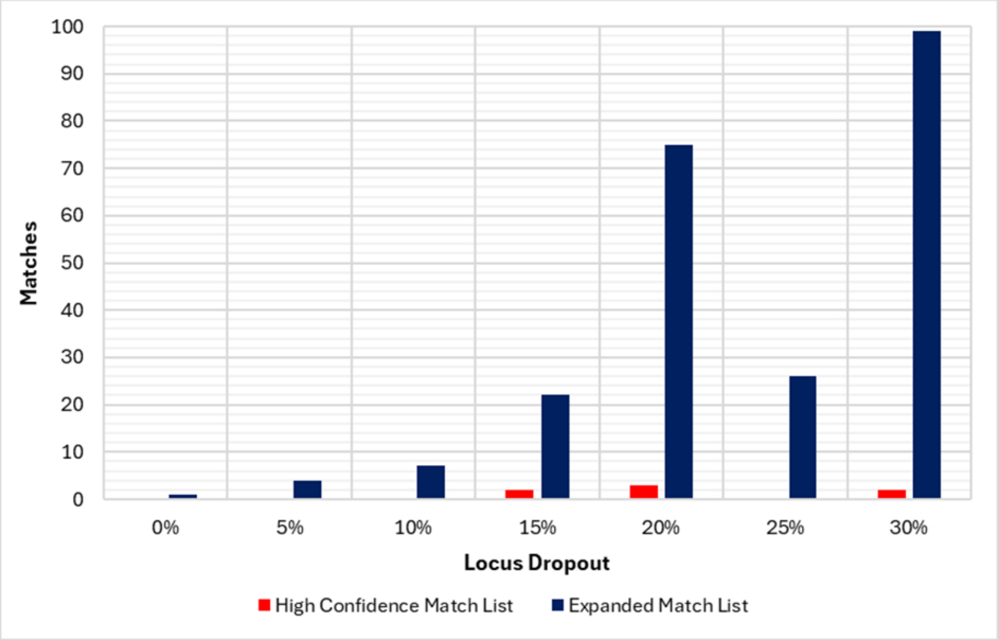

Figure 5. Additional matches included in the high confidence and expanded match lists on GEDmatch PRO™ that were not known genetic relatives of Individual 1 at various degrees of locus dropout.

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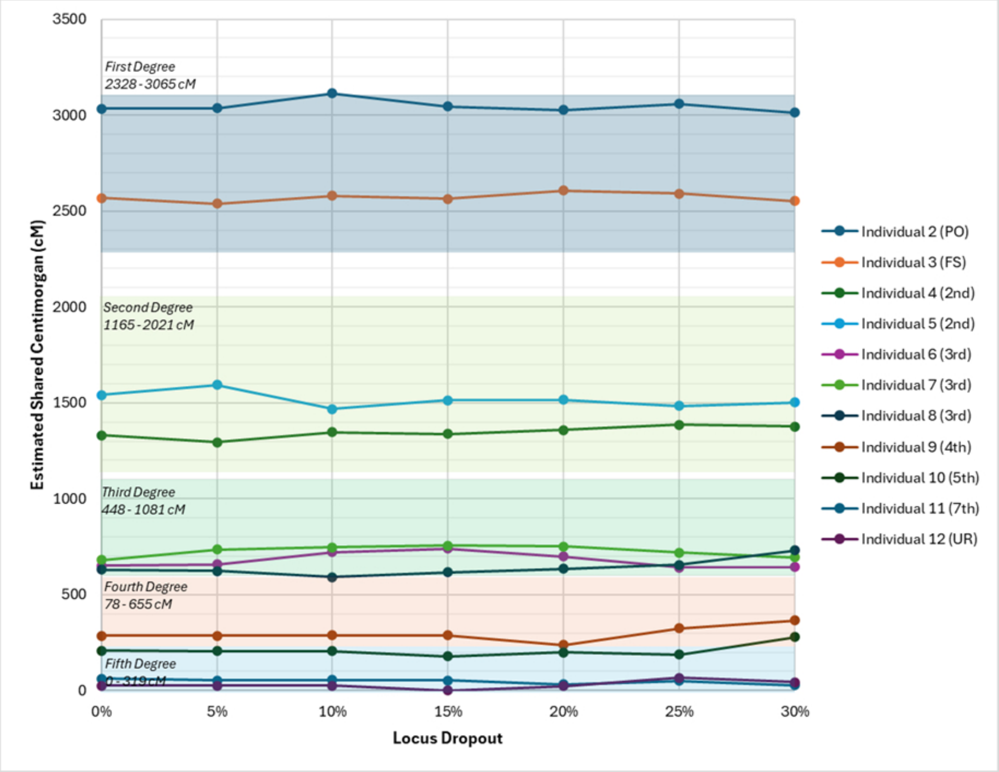

Figure 6. Estimated shared centimorgan (cM) values shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with locus dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.12 PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

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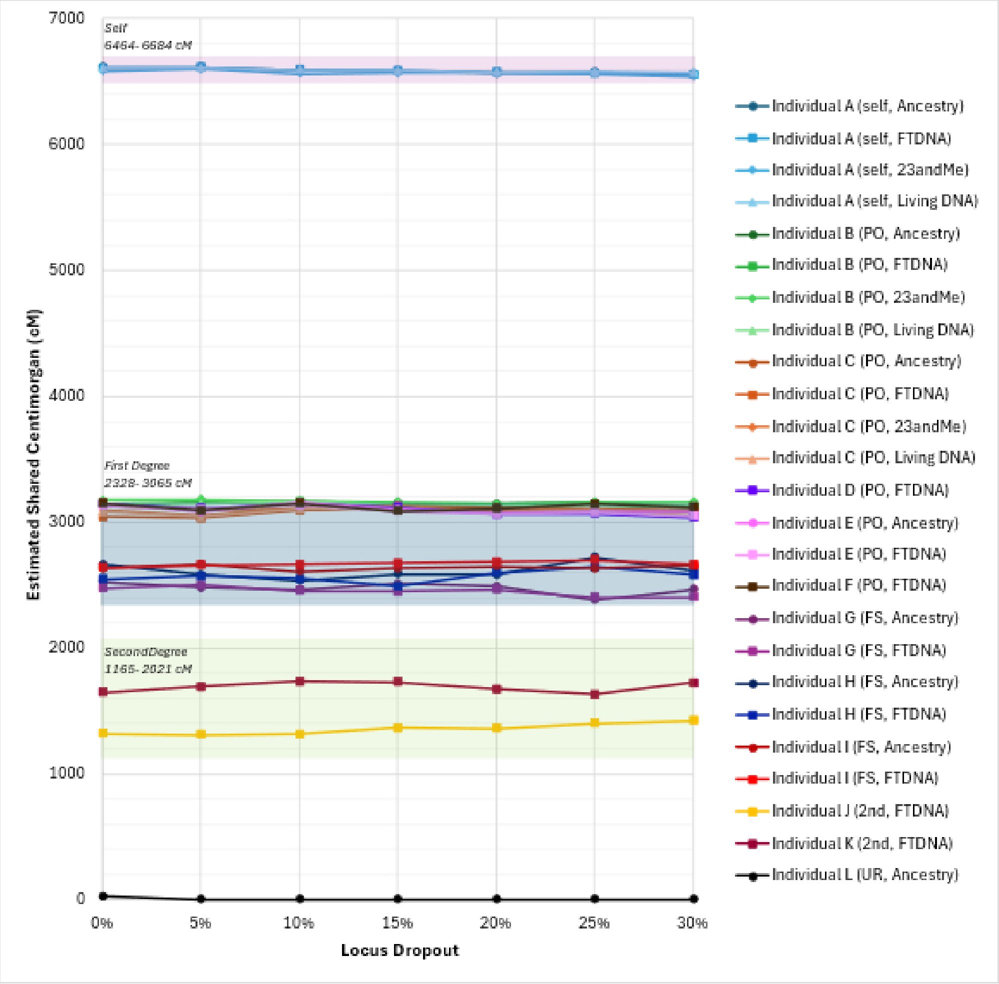

Figure 7. Estimated shared centimorgan (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with locus dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.12 PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

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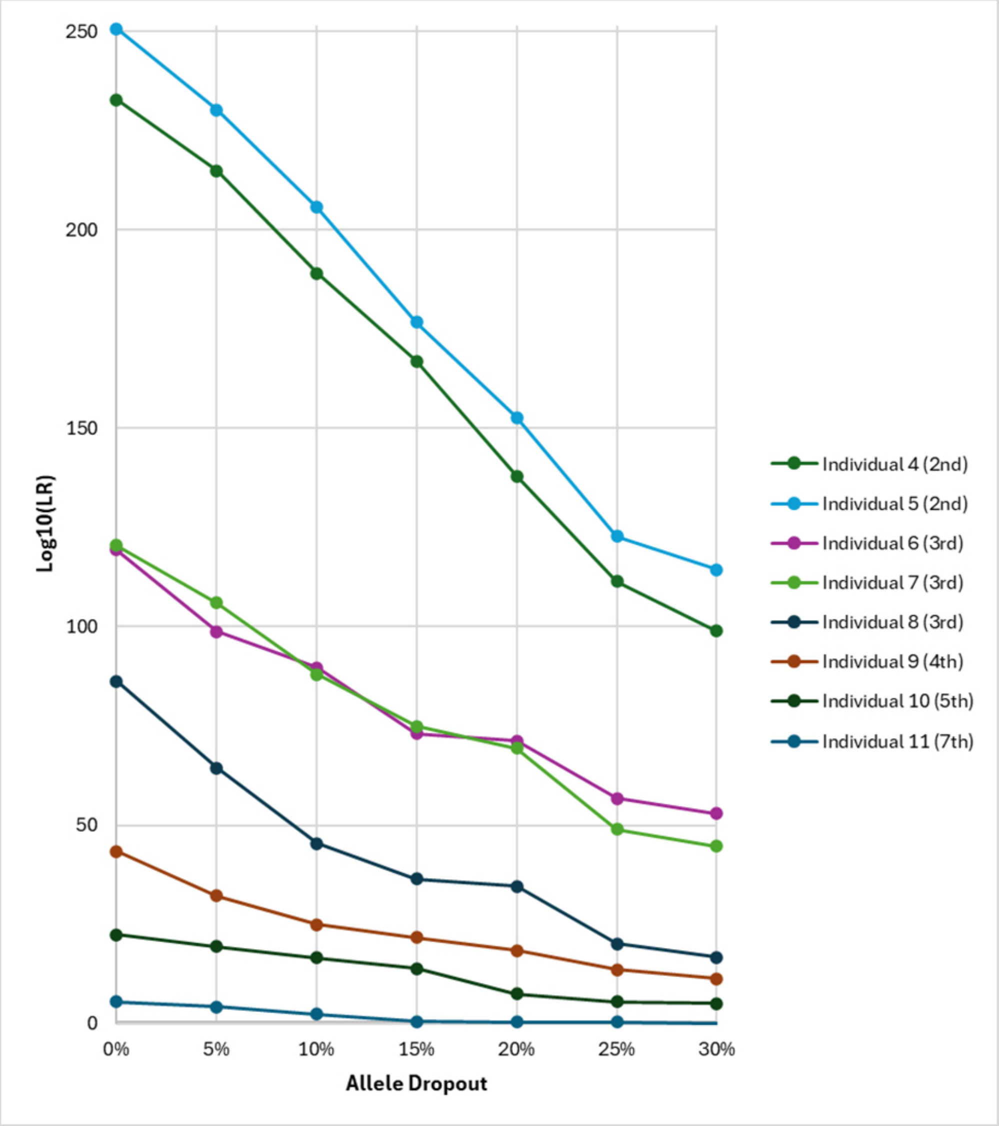

Figure 8. Log10 LRs generated with allele dropout of Individual 1 ranging from 0 to 30% for all true relationships in Pedigree Group 1. The H1 proposition was that the pair were related according to the true relationship degree. The H2 proposition was that the pair were unrelated. The parent/offspring was not plotted (log10 LR = -∞). The full sibling has not been plotted (log10 LR = ∞). 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative.

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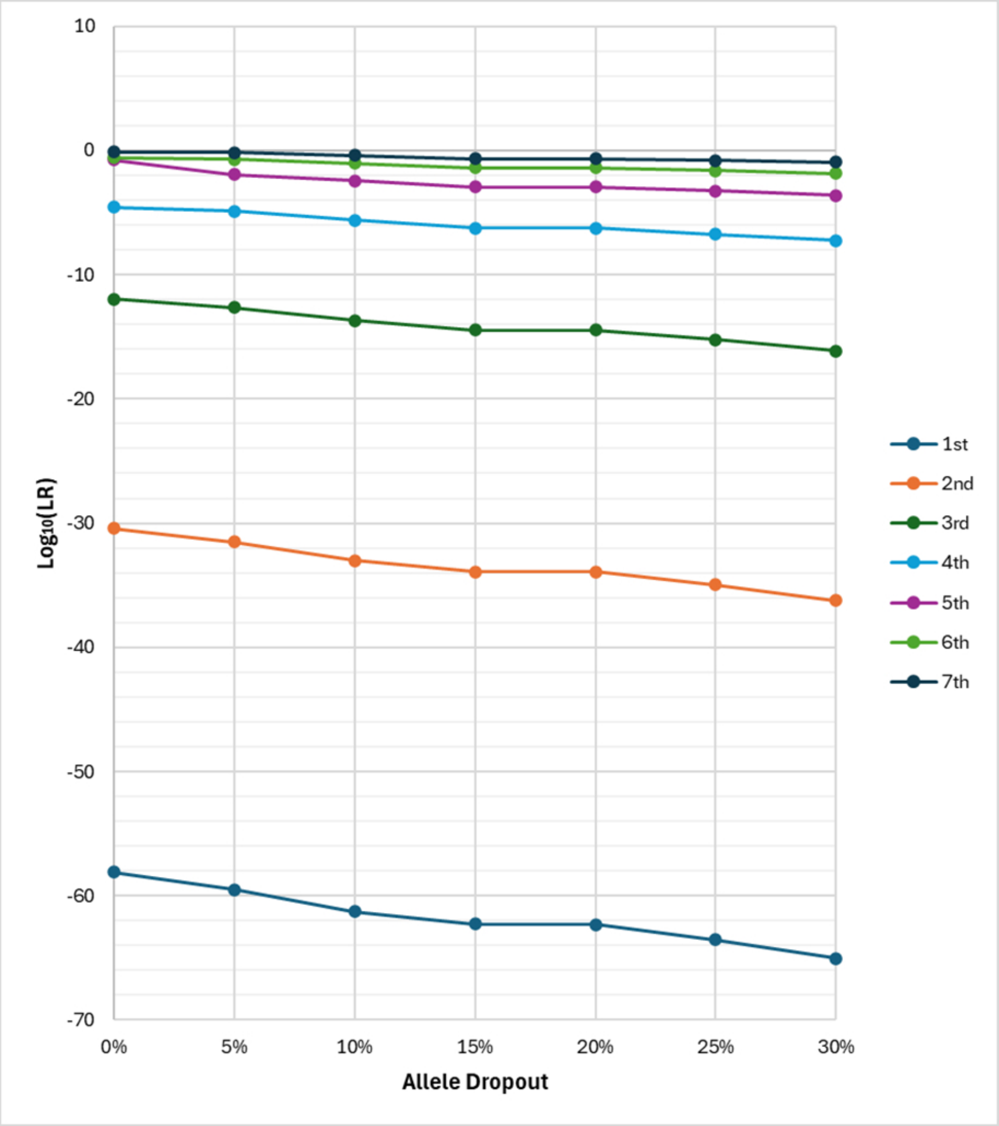

Figure 9. Log10 LRs generated with allele dropout of Individual 1 ranging from 0 to 30% and a true unrelated individual (Individual 12). The H1 proposition was that the pair were related according to a specific relationship degree. The H2 proposition was that the pair were unrelated (true). Parent/offspring tests have not been included as (log10 LR = -∞). 1st: first degree relative; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 6th: sixth degree relative; 7th: seventh degree relative.

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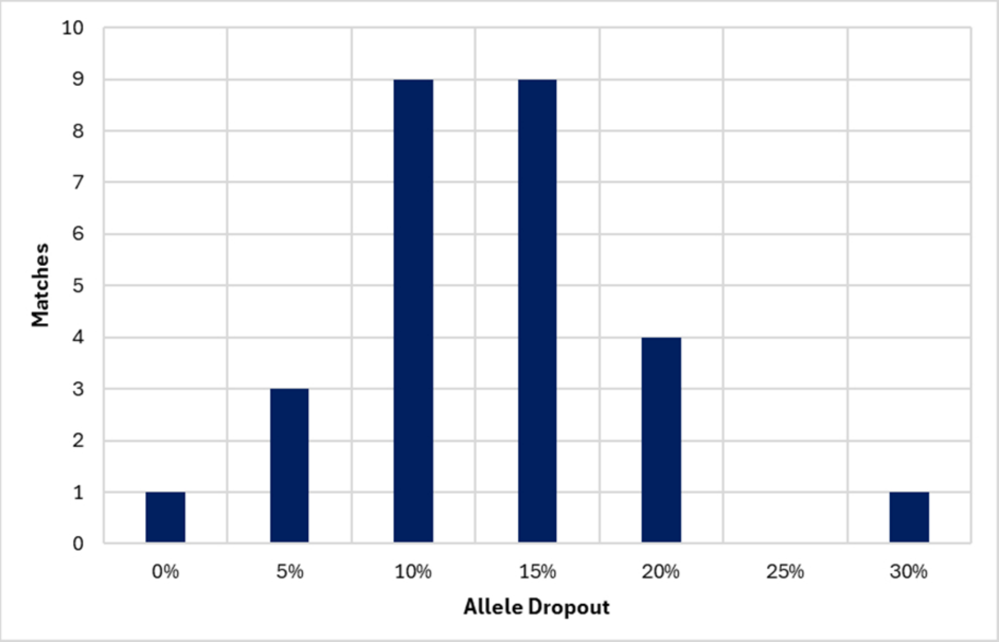

Figure 10. Additional matches included in the expanded match list on GEDmatch PRO™ that were not known genetic relatives of Individual 1 at various degrees of allele dropout.

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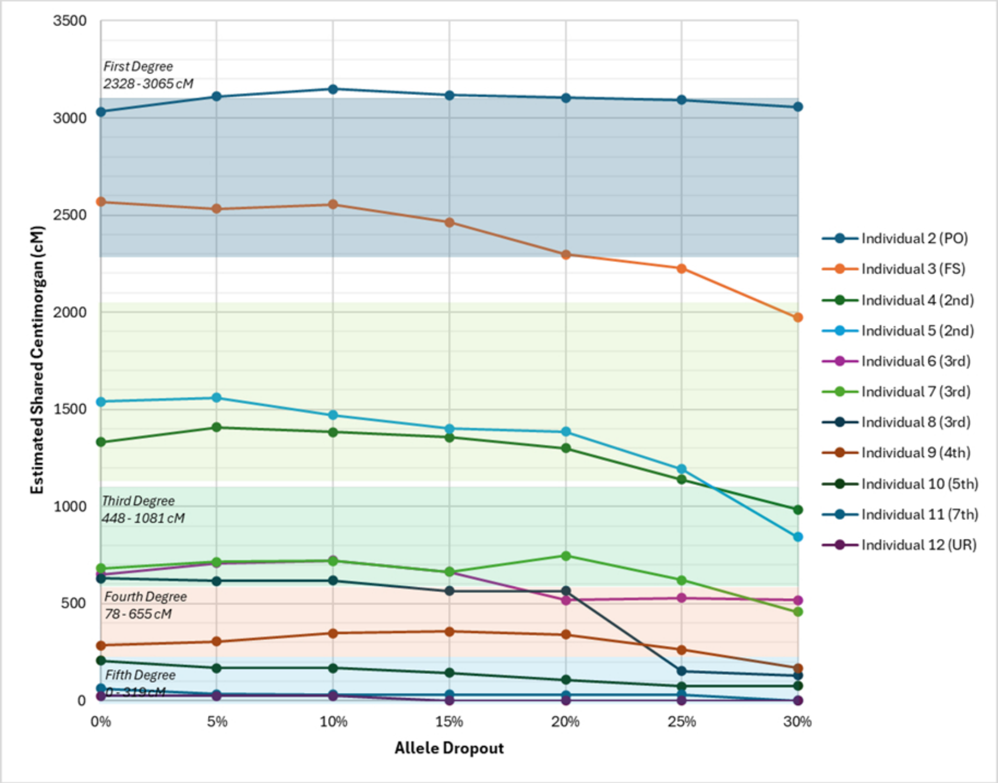

Figure 11. Estimated shared centimorgan (cM) values shared between the Kintelligence profile of Individual 1 and other Kintelligence profiles in Pedigree Group 1 with allele dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.12 PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

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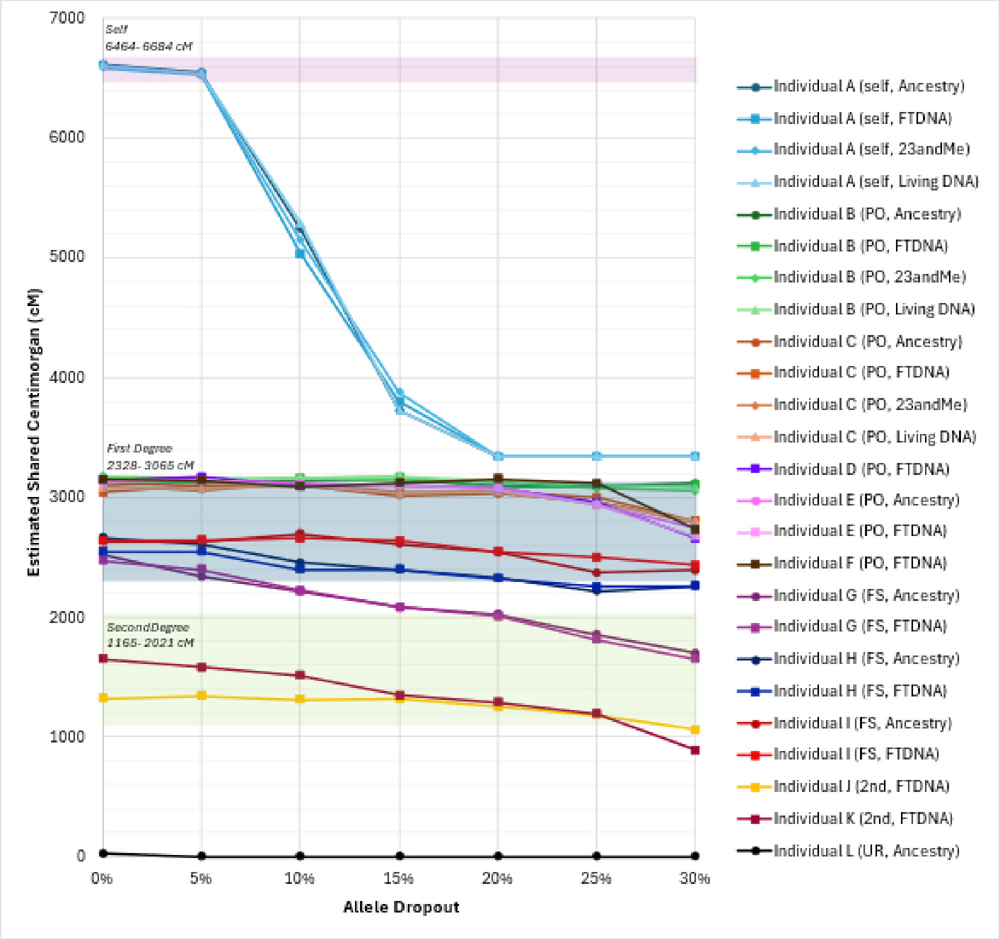

Figure 12. Estimated shared centimorgan (cM) shared between the Kintelligence profile of Individual A and direct-to-consumer profiles in Pedigree Group 2 with allele dropout ranging from 0 to 30%. The ranges indicated for kinship degrees are as included in the generation chart on GEDmatch PRO™.12 PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

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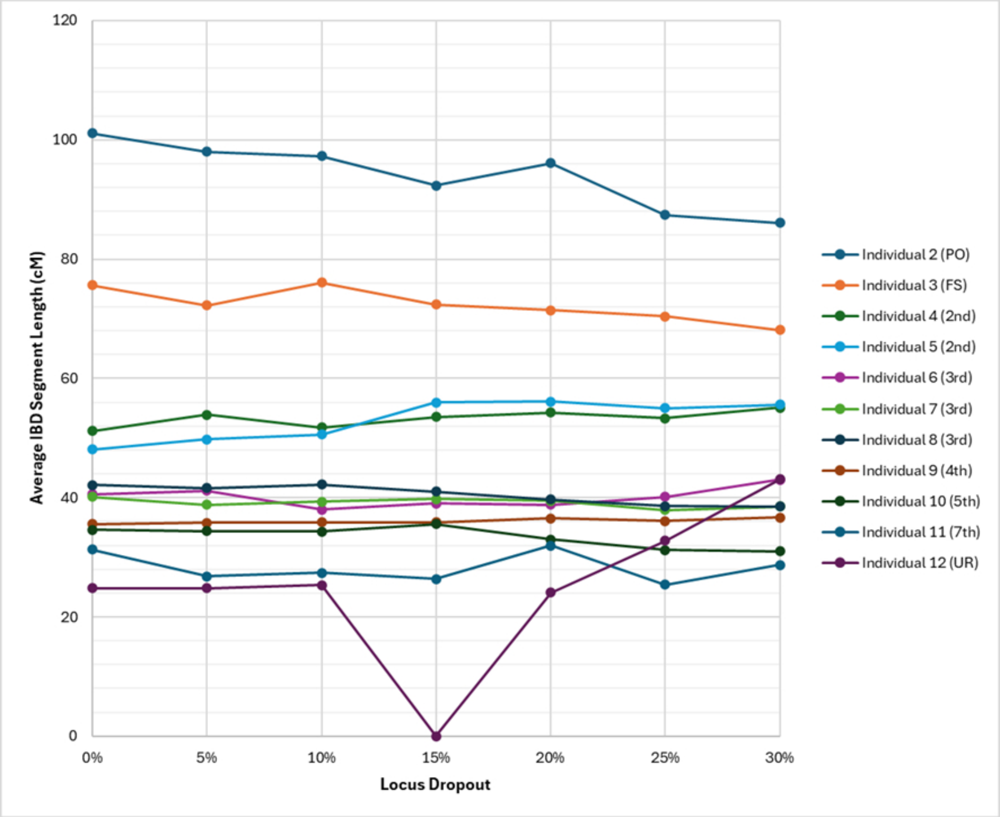

Figure S1. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual 1 with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

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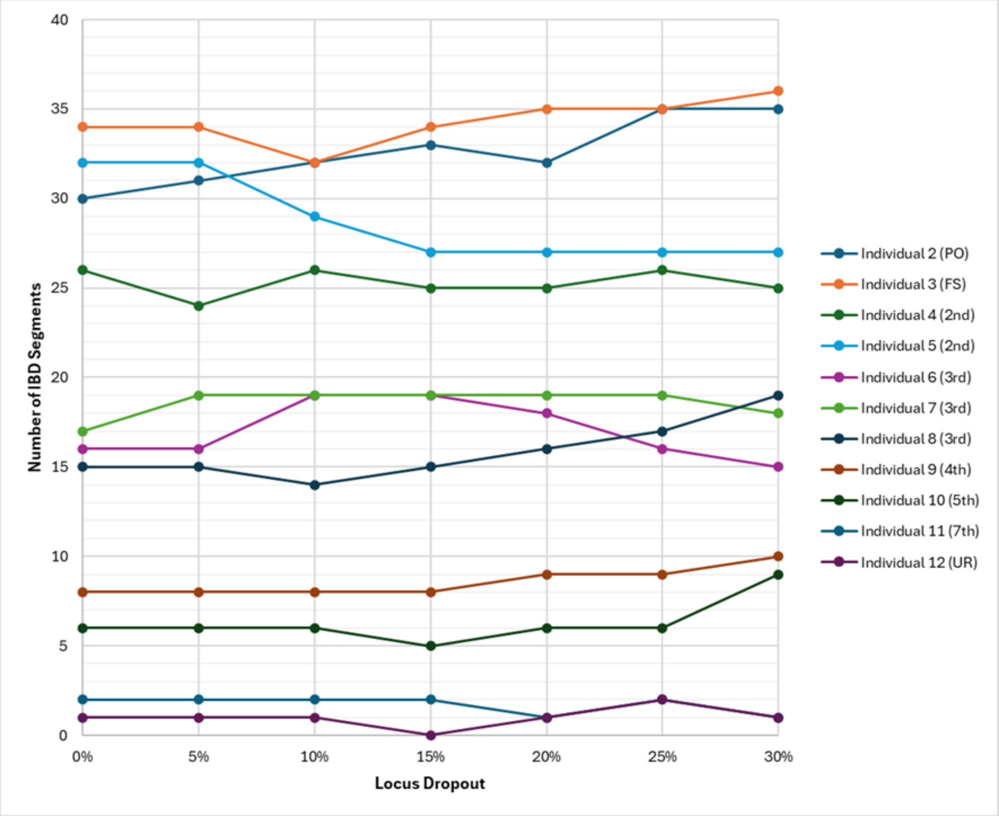

Figure S2. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual 1 with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

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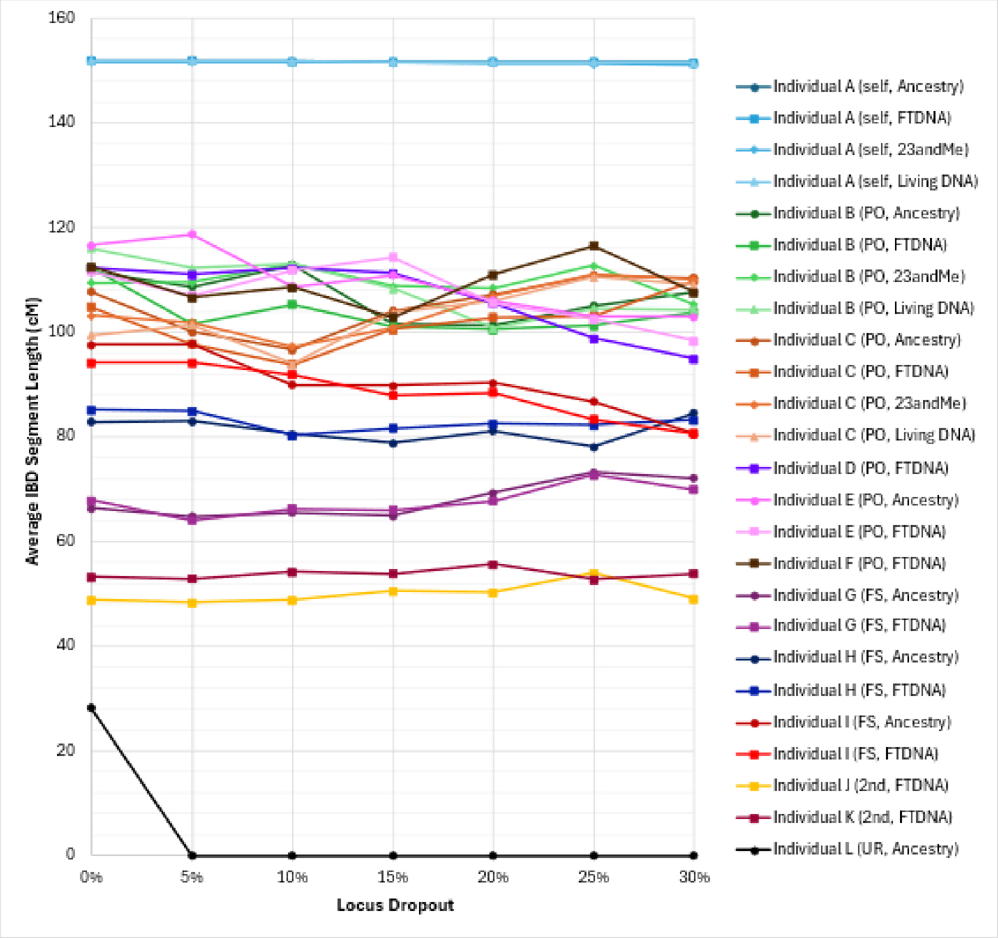

Figure S3. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual A with locus dropout ranging from 0 to 30% and the direct-to-consumer profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

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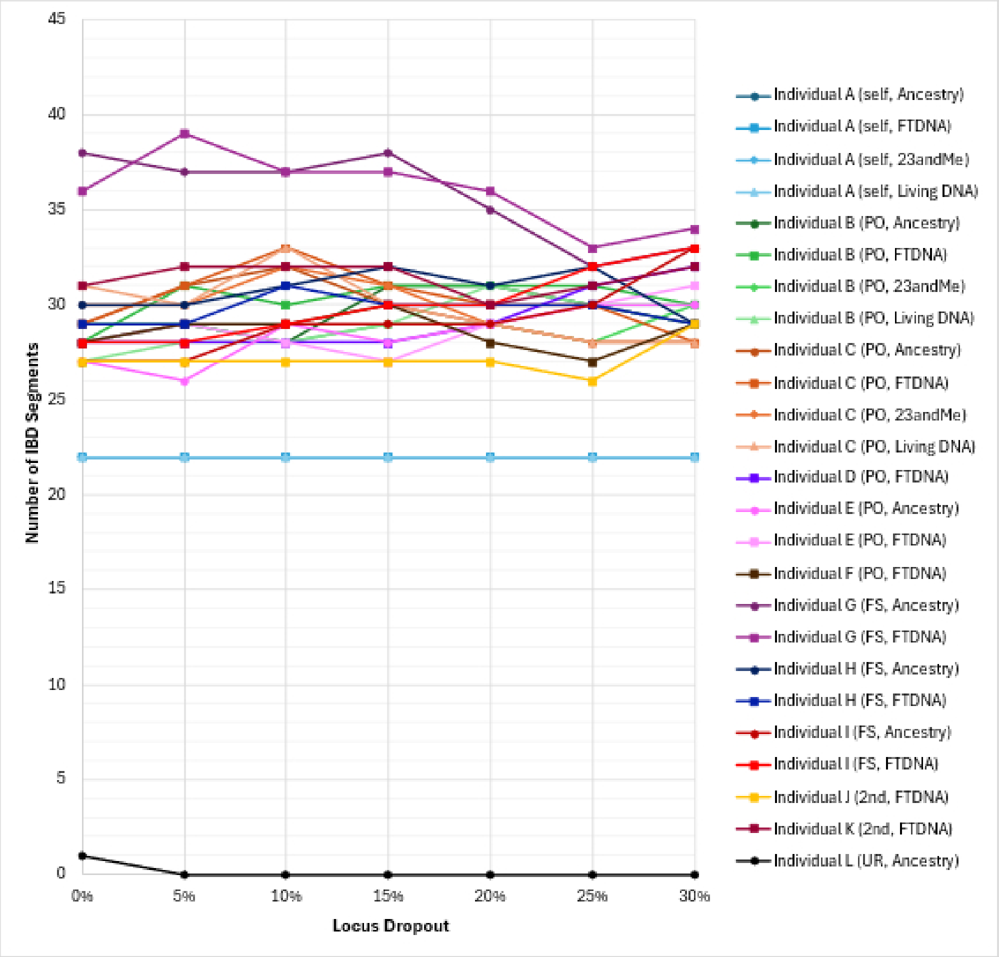

Figure S4. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual A with locus dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

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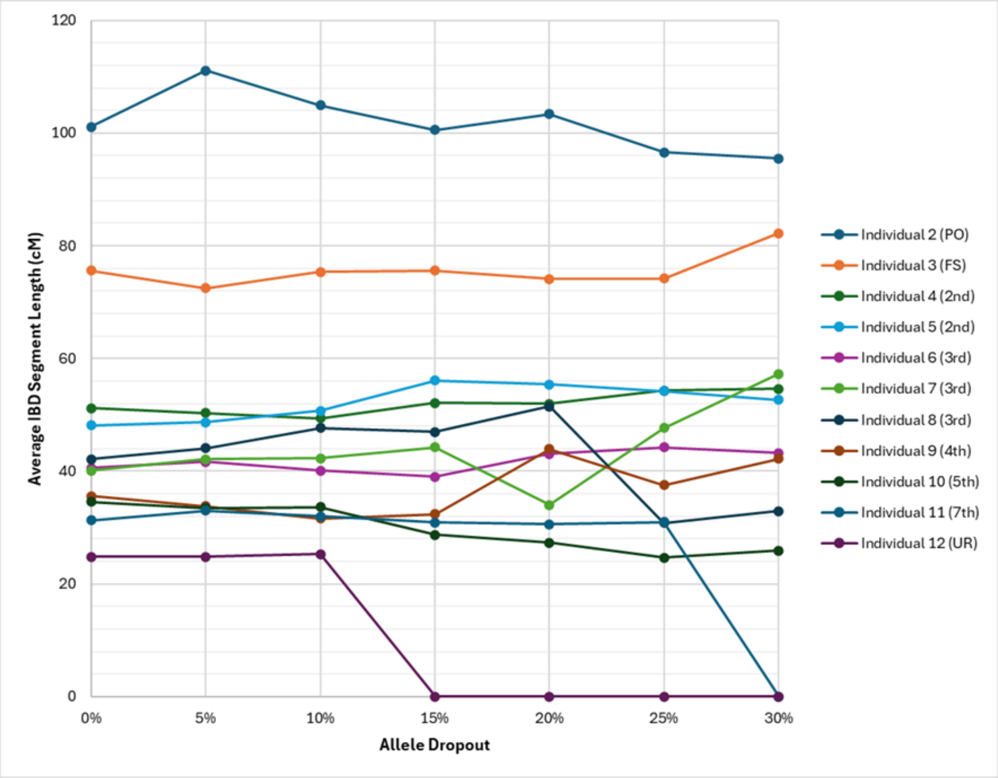

Figure S5. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual 1 with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

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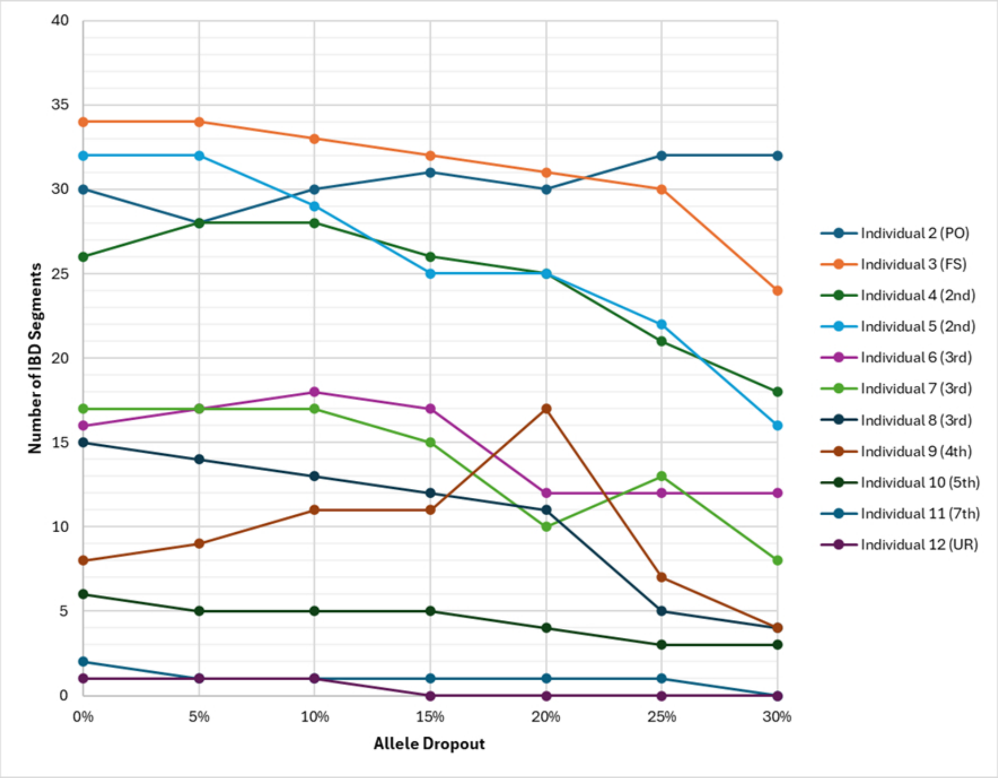

Figure S6. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual 1 with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 1. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; 3rd: third degree relative; 4th: fourth degree relative; 5th: fifth degree relative; 7th: seventh degree relative; UR: unrelated.

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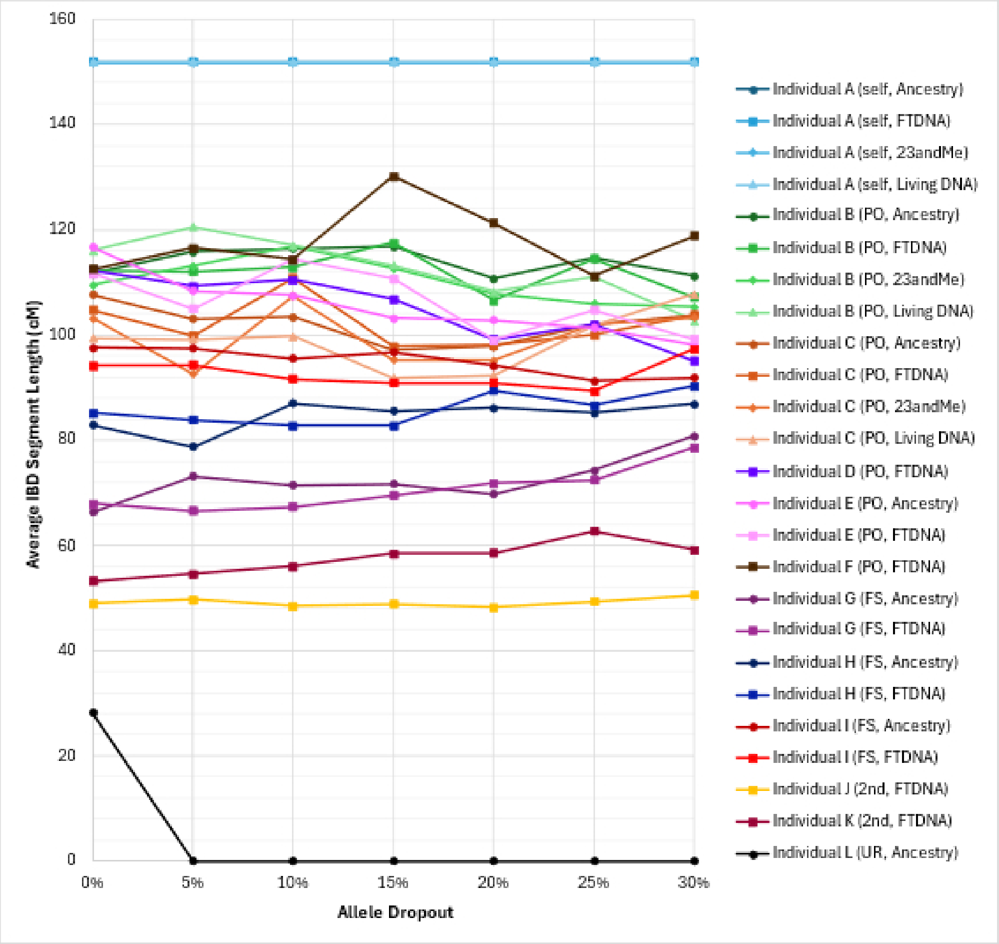

Figure S7. Average identical-by-descent (IBD) segment lengths in centimorgans (cM) between the Kintelligence profile of Individual A with allele dropout ranging from 0 to 30% and the direct-to-consumer profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

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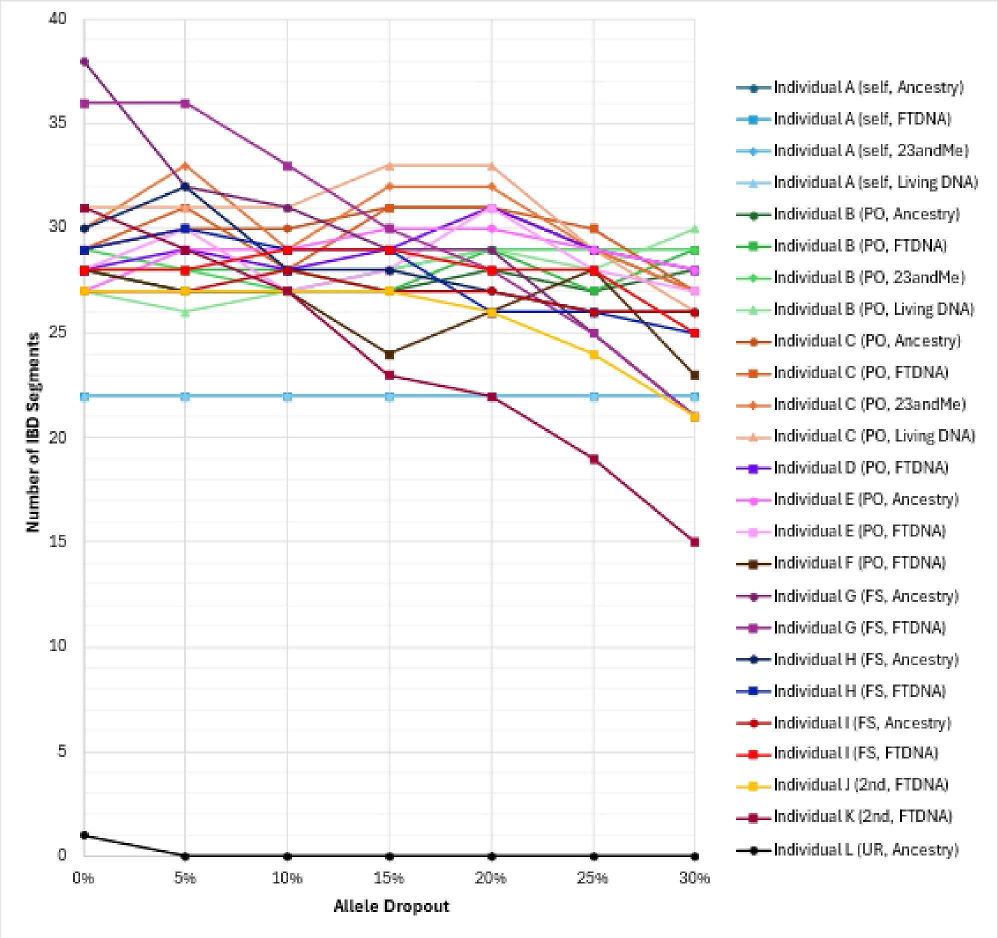

Figure S8. Number of identical-by-descent (IBD) segments detected by GEDmatch PRO™ between the Kintelligence profile of Individual A with allele dropout ranging from 0 to 30% and the Kintelligence profiles from individuals in Pedigree Group 2. PO: parent/offspring; FS: full sibling; 2nd: second degree relative; UR: unrelated; FTDNA: FamilyTreeDNA.

150x141mm (96 x 96 DPI)