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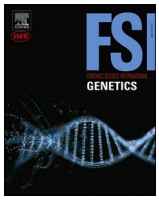

Value of DNA mixture-to-mixture comparisons within an operational context

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ABSTRACT

Since 1995, national forensic DNA databases have used a maximum number of contributors, and a minimum number of loci to reduce the risk of providing false leads. DNA profiles of biological traces that do not meet these criteria cannot be loaded into these databases. In 2023, about 10 % of more than 15,000 trace DNA profiles analyzed in western Switzerland were not compared at the national level, even though they were considered to be interpretable, mainly because they contained the DNA from more than two persons. In this situation, police services can request local comparisons with DNA profiles of known persons and/or with other traces, but this occurs in only a small proportion of cases, so that DNA mixtures are rarely used to help detect potential series. The development of probabilistic genotyping software and its associated tools have made possible the efficient performance of this type of comparison, which is based on likelihood ratios (LR) rather than on the number of shared alleles.

To highlight potential common contributors for investigation and intelligence purposes, the present study used the mixture-to-mixture tool of the software STRmix v2.7 to compare 235 DNA profiles that cannot be searched the Swiss DNA database. These DNA profiles originated from traces collected by six different police services in 2021 and 2022. Traces were selected by the police based on information that indicated that they were from potential series. Associations between profiles were compared with expected investigative associations to define the value of this approach. Among the 27,495 pairwise comparisons of DNA profiles, 88 pairs (0.3 %) showed at least one potential common contributor when using a LR threshold of 1000. Of these 88 pairs, 60 (68.2 %) were qualified by the police services as "expected" (60/88), 22 (25.0 %) as "possible", and six (6.8 %) as "unexpected". Although it is important to consider the limits of this approach (e.g., adventitious or missed associations, cost/benefit evaluation, integration of DNA mixture comparison in the process), these findings indicate that non CODIS loadable DNA mixtures could provide police agencies with information concerning potential series at both the local and national level.

1. Introduction

In 1995, the first DNA database (DNADB) was established in the UK [1]. Two years later, the Council of the European Union invited its member states to consider establishing DNADBs, with these databases subsequently becoming an essential tool to provide investigative leads [2,3]. In general, DNADBs compare at least two groups of items or indices: one index for DNA profiles recovered from biological traces (i.e., forensic unknown) and a second index for DNA profiles from references (i.e., known persons), consisting generally of convicted offenders, as well as suspects in some countries. Comparisons between these indices can result in contributing to associate DNA profiles with their potential sources [4]. In addition to comparisons with persons of interest, scene DNA profiles can be compared with each other to help detect crime patterns. In addition to providing useful investigative leads on a case-by-case basis, this information can also help understand crime phenomena [5–7].

In most countries, specific legislation is required to regulate the types of DNA profiles that may or not be included in DNADBs depending on the type of offence. Moreover, because the risks of adventitious associations increase with more common profiles, when the DNA is from multiple contributors, and with the size of the DNA database, DNA

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profiles generally need to respect various criteria to be uploaded into a database [8]. These criteria vary among databases and countries, but DNA profiles usually must include a minimum number of alleles or loci, or a maximum conditional profile probability, and a maximum number of contributors [9,10]. In Switzerland for example, the only DNA profiles that can be sent to the national DNADB are those from one contributor (single or major contributor) involving at least six loci, and profiles of mixtures from a maximum of two contributors, involving at least eight loci. By contrast, interpretable mixtures from more than two contributors cannot be sent to the national DNADB [11]. Once loaded into the database of the Swiss Combined DNA Index System (CODIS), the profiles can be compared using different stringency modes. The comparison of DNA profiles from references and biological traces is efficient, but the comparison of DNA mixtures is not: all alleles must be identical to establish a potential association between two-person mixtures. Thus, both DNA mixture profiles must share exactly the same allelic content to report an association.

Trace DNA represents a large proportion of the scene items currently analysed. For example, 88 % of the over 15,000 scene items analysed in western Switzerland in 2023 were trace DNA (i.e., 12 % were described by the police as blood, semen or saliva). These traces usually contain low quantities of DNA and are often from several individuals. Resulting DNA profiles are frequently partial and/or mixed. Thus, many of these profiles cannot be transmitted to a DNADB and cannot be compared systematically to potential candidates or to other scene DNA profiles. For example, interpretable DNA profiles were obtained for 55 % of the over 15,000 traces processed in western Switzerland in 2023. The remaining DNA profiles could not be used because of their poor quality or complexity (i.e., replicates were not reproducible and/or there were more than eight alleles at several loci). The interpretable DNA profiles can be divided into those that meet the criteria for uploading into the Swiss national DNADB, being from one or two persons and accounting for 45 % of the traces analysed; and those that cannot be transmitted to the DNADB, mainly because they come from more than two persons and accounting for 10 % of the traces analysed. Police services can occasionally request the laboratories to compare DNA profiles from traces with DNA profiles of given persons. However, this requires that a person of interest has already been suggested by the investigation. Alternatively, trace profiles can be compared with the national DNADB one time and without being uploaded (one-off searches). These options, however, are time consuming and are utilised in only a small proportion of cases. In addition, profiles of DNA mixtures are rarely compared with each other. Thus, it is not possible to use these profiles to detect potential series without investigative information. This represents a loss of information as well as a financial loss to the judicial system as these profiles were analyzed but only partially used.

The development of probabilistic genotyping (PG) has made possible the more effective use of these mixed DNA profiles. PG, which was developed in response to the increasing complexity of DNA profiles [12,13], incorporates a combination of mathematical processes and biological modelling that enables DNA profiles from multiple contributors to be exploited, even when the quantity and/or quality of DNA is suboptimal [13]. PG computes likelihood ratios (LR) to determine the value of the DNA comparison taking into account the number of contributors and stochastic variations within the DNA profiles such as drop-out and drop-in [14]. PG can also be used to compare a DNA profile with a database [15]. In these situations, the LR assigned when comparing the DNA profile of a trace with those of references is usually the ratio of the probability to observe the results if the candidate has contributed to the DNA mixture divided by the probability of the results if unknown persons, unrelated to the candidate, have contributed to the DNA mixture. PG can also be used to compare mixture DNA profiles with each other to help determine if one or several persons have contributed to both mixtures [16,17]. In this situation, the LR is the ratio of the probability of observing the results if the DNA mixtures have at least one contributor in common divided by the probability to observe the same profiles if both DNA mixtures have no contributor in common. The usefulness of mixture-to-mixture analyses has recently been illustrated in studies investigating their potential to detect contamination between analysed traces [18] as well as to gather large scale intelligence data [19].

The present study used the mixture-to-mixture tool of the software STRmix v2.7 to compare casework DNA mixture profiles provided by several police services of western Switzerland to highlight potential common contributors. The aims of this study were to determine the value and limitations of this type of approach by comparing the associations supported by these analyses with those suggested by the police services using other forensic or situational information.

2. Material and methods

To investigate the potential of the mixture-to-mixture tool of STRmix™ V2.7 (https://www.strmix.com/strmix/) to highlight possible common contributors to trace DNA profiles, each of the six French-speaking police services in western Switzerland was asked to select 20–60 DNA profiles from traces collected between 2021 and 2022 that did not meet the criteria to be sent to the Swiss DNADB. The investigators were asked to select traces based on information indicating possible involvement of the same individuals. No other criteria were provided for the selection of these traces.

A total of 235 complex DNA profiles were selected by the police services (Table 1). These DNA profiles were obtained following standard procedures of our laboratory (available upon request). In summary, template DNA (0.5 ng or a maximum of 10 µl in a total reaction volume of 25 µl) was PCR amplified with 30 cycles using a 16 loci AmpFLSTR™ NGM SElect™ PCR Amplification Kit (ThermoFisher Scientific, Reinach, Switzerland). The DNA from each item was analysed at least twice, as required by Swiss law. The number of contributors assigned to these DNA profiles varied from one to four, with this number based on all the replicates available, as well as the numbers of peaks and their height. The DNA profiles were deconvoluted and compared using STRmix™ V2.7 software. In addition, the results of STRmix diagnostics (e.g., log (likelihood), mixture proportions, RFU per contributor, and potential drop-in alleles) were checked to verify that they were not in contradiction with the number of contributors assigned and that results were intuitive [20]. Of the 235 profiles, 129 (54.9 %) and 99 (42.1 %) were assigned as from three and four persons, respectively. Although one (0.4 %) and six (2.6 %) DNA profiles were assigned as from one and two contributors, respectively, they did not have the minimum number of loci required to be transmitted to the Swiss DNADB. The DNA profiles of five contributors were not included, as we had only validated STRmix for a maximum of 4 contributors at the time of this study.

All 235 deconvolutions were compared with each other using the mixture-to-mixture tool of STRmix v2.7 software. Therefore, the traces from all police services were compared together even when the traces were not from cases that were believed to be linked. Based on the number of comparisons involved and preliminary tests (see supplementary Figure 1), a LR threshold of a thousand was considered a good trade-off between the number of leads proposed and the probability of detecting an association when present. Only pairs of profiles having LRs $\geq$1000 were further explored.

The results of mixture-to-mixture comparisons were transmitted to the corresponding police services, without mention of LRs to prevent bias. Each police service was then requested to classify the possible association as: (i) expected, if other forensic information (e.g., fingermarks, footwearmarks, mobile phone records) supported an association; (ii) possible, if the *modus operandi* were similar but the other information was limited; (iii) unexpected, if cases were of a different type, or (iv) unknown, if no information was available.

3. Results

A total of 235 complex DNA profiles from traces supplied by six

Table 1
Number of associations based on a LR threshold ≥1000 between pairs of DNA profiles provided by the six police services (A to F). N = number of profiles submitted by each service. Intra- and inter-police service associations are indicated in orange and green boxes, respectively.

	A	B	C	D	E	F
A (N = 30)	15					
B (N = 47)	1	18				
C (N = 32)	-	-	8			
D (N = 48)	-	-	2	6		
E (N = 20)	-	2	-	-	2	
F (N = 58)	2	-	-	1	-	31

police services in western Switzerland were compared with each other using the STRmix™ mixture-to-mixture tool. Among the 27,495 possible pairwise comparisons, 88 (0.3 %) showed at least one potential common contributor with LRs ≥1000 (Table 1). Eighty of these pairs consisted of DNA profiles supplied by the same police service, accounting for 1.6 % of the intra-police service comparisons, and 8 pairs consisted of DNA profiles supplied by different police services, accounting for 0.03 % of the inter-police service comparisons. In total, 103 DNA profiles were associated with at least one other profile, generating 34 groups of 2–7 profiles (Fig. 1).

Because the DNA profiles analysed in this study were from ongoing cases, it was not possible to determine whether the associations detected by the mixture-to-mixture tool were adventitious or not. The associations revealed by these mixture-to-mixture analyses were therefore compared with police expectations. Of the 88 mixture-to-mixture associations, 60 (68.2 %) were classified by the police services as "expected", 22 (25.0 %) as "possible" and only six (6.8 %) as "unexpected". None was classified as "unknown". Four out of the six unexpected

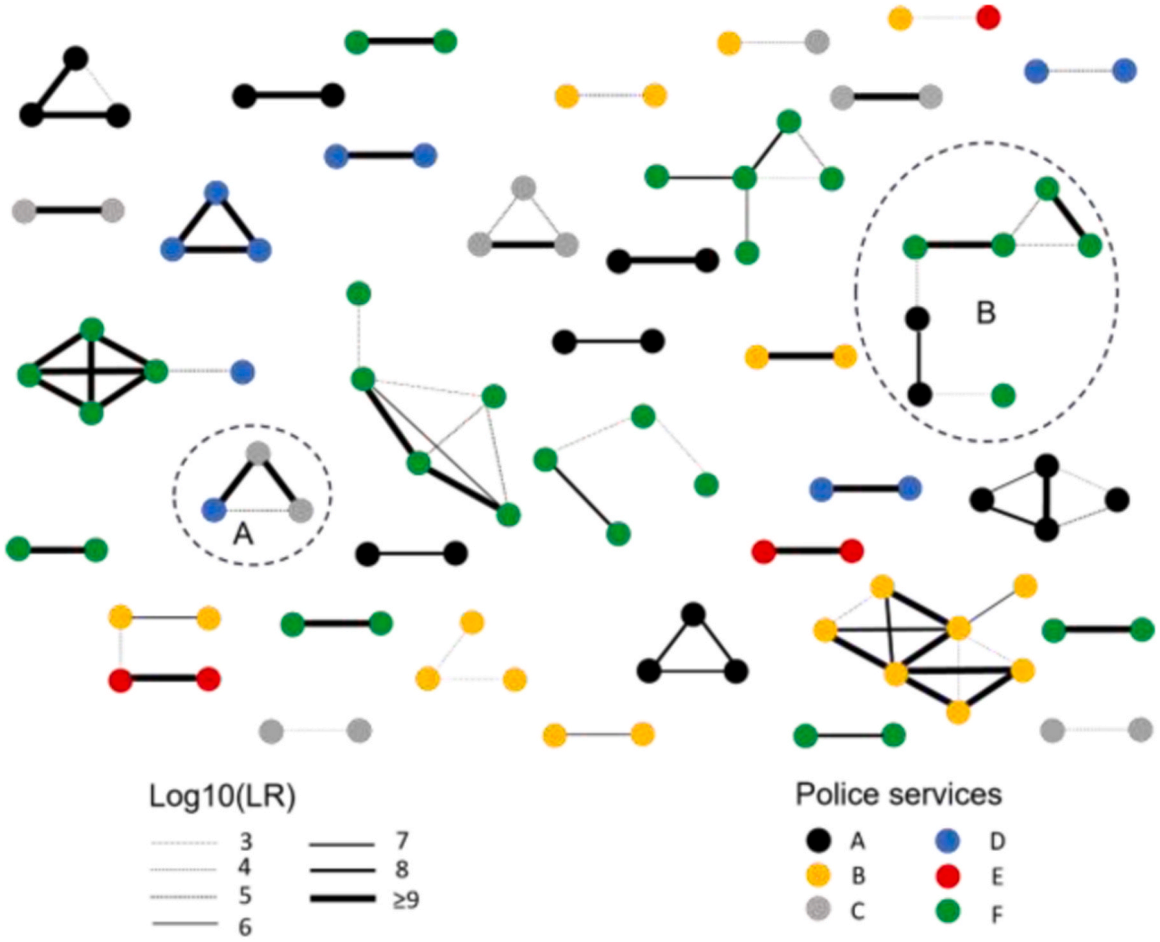

Fig. 1. Schematic representation of the possible associations (represented as lines) recovered using mixture-to-mixture analysis of the DNA profiles (represented as dots). The colour of the dots represents the six police services, and the type/width of lines represents the log10(LR) values of the associations. The two groups A and B are discussed in more detail in the text and in Fig. 3.

associations concerned DNA profiles from different police services. The four other inter-police service comparisons were classified as possible. On five occasions, a police service reported "expected" associations that were not detected by the present analysis.

The distribution of the Log10(LR) values of the 88 associations and their characterisation as "expected", "possible" or "unexpected" are shown in Fig. 2. All six (100 %) unexpected associations had Log10(LR) values ≤ 5 compared with 9/22 (41 %) and 17/60 (28 %) of the possible and expected associations, respectively. Seven of the eight inter-police service comparisons had Log10(LR) values ≤ 5 and one had a Log10 (LR) ≥ 9. Finally, five of the 65 expected associations were not reported by the mixture-to-mixture analysis.

4. Discussion

This large-scale mixture-to-mixture analysis of DNA profiles that did not meet the criteria for inclusion in the national DNADB highlighted 88 pairs of DNA mixtures sharing at least one potential common contributor. This illustrates the potential of such analyses to provide associations of otherwise unrelated cases based on profiles of DNA mixtures [17–19]. Although the results of the present study could not determine whether these associations were adventitious, as the profiles analysed came from casework, 93 % of the proposed associations were classified by the police services as "expected" or "possible", supporting that most of these associations corresponded to series.

Highlighting possible common contributors to profiles of DNA mixtures using the mixture-to-mixture tool is valuable for several reasons. First, it allows to generate information from DNA profiles that could not be compared using algorithms such as that used by CODIS [13]. Therefore, these possible associations would likely remain undetected. This is typically the case of profiles from different police services or different geographic areas. For example, a comparison of two DNA profiles from Group A in Fig. 1, from police services C and D, resulted in a large LR value (i.e., one billion). This association was characterised as "possible" by the two police services, but no other information was then available to further support this. Although forensic information is sometimes shared among police services to generate intelligence and highlight series of crimes, grouping cases from different police services can be complex and time consuming [5]. The six state police services of western Switzerland share a common crime intelligence database to detect serial offences and to better understand crime phenomena [7]. Procedures have been designed to integrate the associations provided by situational information and forensic data. To date, DNA associations among scenes are detected through the centralised Swiss National DNADB. In this context, the possibility to also detect associations between mixed DNA profiles can provide additional investigative leads. For example, one or several persons of interest may be associated with a single scene on the basis of other investigative leads or of the results of the database search with other trace DNA profiles in this case [19]. The possible involvement of these persons can be further investigated and

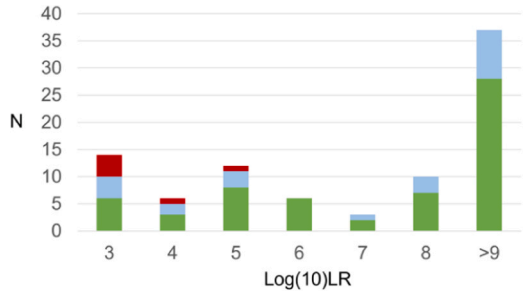

Fig. 2. Analyses of the 88 possible associations revealed by mixture-to-mixture comparisons. Shown are the numbers (N) of associations considered as expected (green), possible (blue) and unexpected (red) by the police services and their log10(LR) values.

their DNA profiles can, for example, be compared with the DNA profiles available in other cases. This can be illustrated by group B of Fig. 1 (detailed in Fig. 3), which includes seven profiles from multiple cases investigated by police services A and F. Two persons were compatible with several DNA profiles, with person A being compatible with profiles of trace 1 through 4 and person B being compatible with profiles of trace 5 through 7, after comparisons requested by the police services. Interestingly, the compatibilities with persons A and B may explain several of the associations detected by the mixture-to-mixture analyses. Nevertheless, these two reference DNA profiles were not compatible with all the DNA profiles of the group, and they likely do not explain the association between profiles of traces 4 and 5. Although this association might be adventitious, its high value (Log10(LR) $\geq$ 9) suggests the presence of at least one possible contributor in common and worth further investigation. In addition, more than one individual may contribute to some mixtures, potentially creating large series among DNA profiles from different cases. In that case, mixture-to-mixture analyses may optimise requests for on-demand comparisons between complex DNA profiles and persons of interest.

DNA profiles at scenes may also contain background or prevalent DNA, such as DNA from victims or from individuals unrelated to the case. Such DNA profiles are not useful for database searches or local comparisons of DNA profiles of persons of interest. Highlighting a contributor common to profiles from different cases suggests that these profiles may contain important information and should be compared with potential suspects in the case. In addition, combining the information contained in two or more associated profiles may help define the possible genotype of an individual common to these mixtures. This information may in turn be used to optimise a one-off database search or at least indicate that the search is pertinent. For example, several DNA profiles from different but potentially related cases were included in this study. Two of these profiles were associated with a large LR (i.e., in the order of one million) suggesting that one individual may have contributed to both. Although these DNA profiles did not satisfy the criteria for loading into the DNADB, each was compared with the profiles in the Swiss national database using a one-off search. Findings indicated a potential association with an individual who had not been suspected. Interestingly, these profiles would likely not have been compared to the database without information about the potential common contributor to the two DNA profiles. As any investigative lead, however, it is important that they should be evaluated in conjunction with other information about the case [21].

Mixture-to-mixture analyses may also be used to gather general intelligence information about crime phenomena [19]. The value of such analyses was illustrated by various studies using single source traces compared to national DNA databases [5,6]. The present study was not designed for this purpose, as the DNA profiles analysed represented fewer than 10 % of the mixture profiles analysed in our laboratory during the study period. Moreover, these DNA profiles were not selected at random: rather, police services were asked to select traces based on information suggesting that they might belong to a series. Therefore, the results of this study overestimate the proportion of associations. The proportion of associations between DNA profiles from the same police service (1.6 %) was higher than the proportion between different police services (0.03 %). This was expected, as each police service represents an individual geographical region, with crimes performed by individuals tending to be geographically localised [19]. Furthermore, these police services likely selected cases that supported intra-service associations, based on accessible situational information, which may have artificially increased the proportion of associations within services.

Finally, some of the associations recovered may be due to contamination events. Contamination might be explained by sample-to-sample transfer of DNA (directly or through consumables) or by transfer of DNA from a person to a sample at any stage of analysis. These contamination events may be revealed by the presence of the same DNA in multiple samples. Mixture-to-mixture analysis could reveal potential

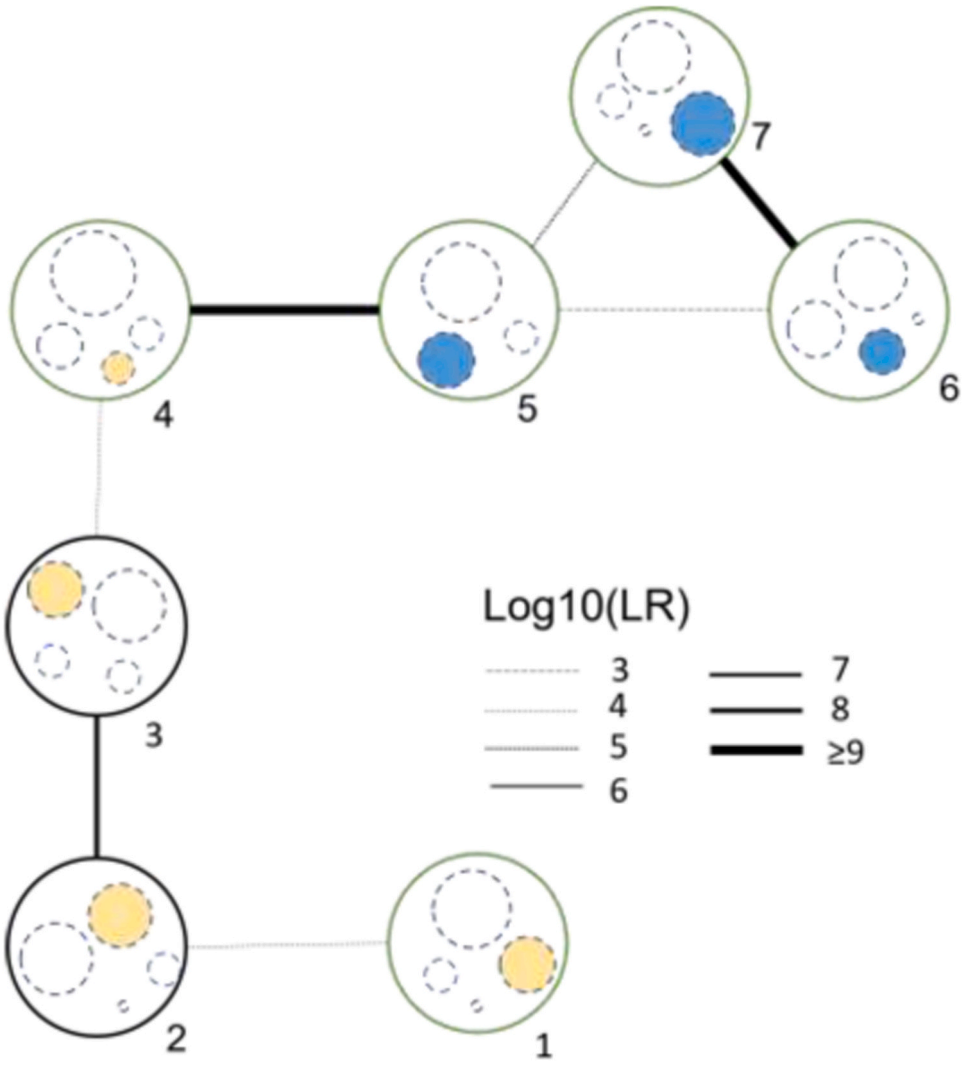

Fig. 3. Detailed representation of Group B in Fig. 1. Each larger circle represents one mixture profile (numbered 1 through 7), whereas the smaller dotted circles represent one contributor to the mixture. The size of these dotted circles is proportional to the mixture proportion proposed by STRmix™ deconvolution. The coloured circles indicate the positions of persons A (yellow) and B (blue) that whose DNA profiled were compatible with parts of the mixture DNA profiles. The type/width of the lines represents the log10(LR) values of the associations.

contamination events and thus be used for quality assurance [18]. Although none of the associations proposed in the present study was clearly associated with a contamination event, contamination can be difficult to detect, especially when it occurs between traces from the same case. In addition, detection of contamination by staff members often requires the comparison of profiles with an elimination database [11]. Mixed profiles are often not subjected to such comparisons, making the proportion of mixture profiles contaminated by staff members currently unknown. Recent data from our laboratory suggest that this proportion is relatively low and of the same order of magnitude as in DNA profiles transmitted to the national DNADB (publication in preparation). This possibility should be considered when investigating an association, especially when it is unexpected.

Although mixture-to-mixture comparisons may be useful in identifying potential common contributors, this type of analysis also has several limitations. First, the possibility of adventitious associations should be considered whenever performing a large number of comparisons [17,19]. The number of adventitious associations is dependent on both the number of comparisons and the LR threshold set to recover associations. A higher number of comparisons and a lower LR threshold value increases the risk of adventitious associations. Regardless of the threshold, however, the possibility of an adventitious association should always be considered. The choice of LR threshold should be based on multiple factors such as prior odds of associations, the probability of detecting an association when one is present, the number of false associations that would be investigated, the seriousness of the cases investigated and the resources available to investigate potential associations, and the consequences associated to the decision regarding the threshold value (detection of a real association, detection of an adventitious association, non-detection of a real association and non-detection of an adventitious association). In addition, these mixture-to-mixture analyses should be considered in an investigative context. It is therefore not possible to define a clear threshold that should be used for all mixture-to-mixture analyses. Rather, the threshold should be adapted to the various type of situations encountered considering the factors mentioned earlier. For example, in situations of systematic comparisons of DNA profiles for intelligence purposes a standard LR threshold of one million might be considered as appropriate as recently illustrated [19]. In contrast, in situations of comparisons of few profiles from sensitive cases, such as serial homicides or sexual assaults, it may be relevant to lower this threshold to help develop leads in the absence of other enquiry information [17]. This lower LR threshold will statistically also generate more adventitious associations, but this is not an issue as long as investigators are aware of this possibility and that the number of leads

remains acceptable in relation to resources.

The present study set the LR threshold relatively low, at 1000, as this was considered a good trade-off between the number of leads proposed and the probability of detecting an association when one is present. In addition, because police services were asked to select traces based on investigative information indicating some associations, their prior probability for associations were rather high. Hence, in such situations, lower LR values may be appropriate to highlight possible associations. A total of 27,495 pairwise mixture-to-mixture comparisons were performed, resulting in more than 300,000 LR calculations between each contributor of these mixtures. Based on the numbers of comparisons and these LR values, multiple adventitious associations were expected. Here, as in all real cases, it was not possible to clearly determine whether a link was adventitious or not. Each police service was asked to classify associations as "expected", "possible", "unexpected" or "unknown" without knowing the results of DNA comparisons. The distinctions between these categories might depend on the person who evaluated the associations, suggesting caution in evaluating these distinctions. None of the associations was categorised by the police services as "unknown", indicating that investigative information was sufficient to classify them. Associations reported by the police as "unexpected" were those where no other elements supported a possible association. Interestingly, all six "unexpected" associations had Log10(LR) values ≤ 5 indicating that setting a larger LR threshold, at, for example, one million, would have excluded these potentially adventitious associations. However, 9 (41 %) and 17 (28 %) of the "possible" and "expected" associations, respectively, had Log(LR) values ≤ 5, indicating that setting the threshold at one million threshold would have missed these associations.

Only five associations expected by the police services (out of a total of 65 expected association) were not detected by the mixture-to-mixture analysis. These associations were expected by the police because a same person was possibly associated with several DNA profiles, but the associations among the corresponding DNA mixture profiles were not reported. An absence of reported association may be explained because (i) the cases were not associated and therefore did not share a common contributor, (ii) the cases were associated but the profiles did not share a common contributor and (iii) the profiles shared a common contributor but the reported LR was below the fixed threshold. This last situation is illustrated by Group B in Fig. 1, as detailed in Fig. 3. One individual was compatible with profiles from trace 1 through 4, but no direct associations were reported, for example, between profiles from trace 1 and 3, 1 and 4, and 2 and 4. This number of "missed" associations likely represents an underestimation, as similar situations were suggested by the present analysis but were not reported by the police. Reported LRs can be affected by several factors, such as the complexity of the mixtures (i.e., the total number of contributors to the two mixtures), the amounts of DNA present in the mixture, and the relative contribution of each individual to the mixtures (i.e., its balance) [17]. For example, with comparable mixture proportions, the expected LR would be lower when comparing DNA mixtures from four contributors than from two contributors. Similarly, the LR would generally be lower when comparing an individual that aligns with a minor rather than with a major contributor. In addition, the LRs expected with mixture-to-mixture comparisons would be lower than those expected for comparisons of a reference to a mixture [17] because the profile of the known person is complete whereas very little information may be shared by the two mixtures. Although the presence/absence of possible associations between DNA profiles may be useful in prioritising comparisons, it is important to always compare the profile of an individual directly with that of a mixture when other investigative information suggests this individual may have contributed to the mixture.

Large scale mixture-to-mixture comparisons are relatively easy to perform in laboratories that systematically use PG software to deconvolute mixture profiles [18]. In the absence of automation, this process can be time consuming, especially if numerous profiles are involved. For this reason, all DNA mixture profiles are often not deconvoluted, even in laboratories that have access to PG software. In our laboratory, mixture DNA profiles are deconvoluted when an evaluation of the DNA comparison of the trace with a person of interest is requested. A systematic mixture-to-mixture analysis of all profiles would require a complete change in laboratory processes, as well as additional resources. Moreover, these mixture-to-mixture comparisons must comply with regulations. As local databases are not allowed in Switzerland, a systematic mixture-to-mixture analysis would require changes in the Swiss regulatory system and/or would have to be centralised within the national DNADB. This would represent the most advantageous process: it would allow to quickly compare all mixture profiles revealing potentially unsuspected investigative leads even between DNA profiles from traces provided by different police services. In addition, incorporation of PG software directly within the national DNADB would allow to compare those mixture DNA profiles with reference profiles allowing the production of leads early in the investigation [15,22]. Although PG will probably be integrated into each national DNADB in the future, this change will undoubtedly take time. Therefore, an alternative may be to focus on profiles selected locally by a cost-benefit analysis based on the type of cases (e.g., police services and/or the severity of the crime), the number of profiles involved, and the resources available. Each situation and case are different therefore it is difficult to establish strict guidelines on when choosing to perform such an analysis. Nevertheless, profiles from serious cases from different police services sharing the same modus operandi for which few or no profiles have been sent to the national DNADB represent promising candidates to compare using the mixture-to-mixture tool.

In conclusion, the present study showed that PG software has value for the comparison of complex DNA profiles that cannot be sent to the national DNADB. This allows the detection of case-to-case associations and also of potential series by providing information about the potential presence/absence of common contributors. This use of DNA for investigative and intelligence purposes can be maximised, as these profiles represent a non-negligible fraction of the DNA profiles currently analysed. Although it is necessary to consider the limitations of this approach (e.g., adventitious or missed associations), this method can be used to investigate the occurrence of crimes committed by the same individual, based on profiles from several police services and/or geographical regions. Profiles that cannot be sent to the national DNADB should not be discarded. Rather, similarly to profiles from single individuals, they can be compared with databases of potential contributors (e.g. using specialised software [15]), and/or with each other to highlight possible associations that can be used as leads for criminal investigations. Future studies and collaborations are needed to develop methods to integrate the information provided by these DNA profiles into processes for intelligence or investigation.

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CRediT authorship contribution statement

Tacha Hicks: Writing – review & editing, Validation, Methodology, Conceptualization. **Vincent Castella:** Writing – review & editing, Supervision, Resources, Methodology, Conceptualization. **Patrick Basset:** Writing – review & editing, Writing – original draft, Supervision, Methodology, Formal analysis, Conceptualization. **Louanne Toulemont:** Writing – review & editing, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence

the work reported in this paper.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.fsigen.2024.103110.

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