

The importance of using high resolution HLA typing of HLA-B*27 in determining disease association with ankylosing spondylitis

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AIM

- Possession of HLA-B*27 has a strong association with inflammatory rheumatic diseases, most commonly ankylosing spondylitis (AS).
- HLA-B*27 typing is our most requested disease association test, routinely ordered by Rheumatology clinicians.
- Results are reported as either positive/present or negative/absent for HLA-B*27, consistent with current ASHI Proficiency Testing for HLA-B*27
- As of July 2025, over 400 HLA-B*27 alleles have been identified in the IPD-IMGT database. Several Common and Well-documented (CWD) variants are not associated with AS.
- This analysis suggests the importance of reporting the high-resolution typing for HLA-B*27 alleles in determining disease association with AS.

METHODS

- NGS typing was performed 03-2022 to 04-2025.
- NGS typing was performed with CareDX AlloSeq TX 17.1
- Results were interpreted with CareDX AlloSeq Assign software using IPD-IMGT/HLA 3.45.1 to 3.57.0.

RESULTS

- 2,138 samples were analyzed. 123 (5.8%) of those samples had @ least 1 HLA-B*27 allele. **Figure 1** shows the 6 different B*27 alleles observed.
- A subset of the 2,138 total HLA typings (n=389) were ordered for HLA-B*27 typing. 41 (10.5%) samples had @ least 1 B*27 allele. **Figure 2** shows the 5 different HLA-B*27 alleles observed.

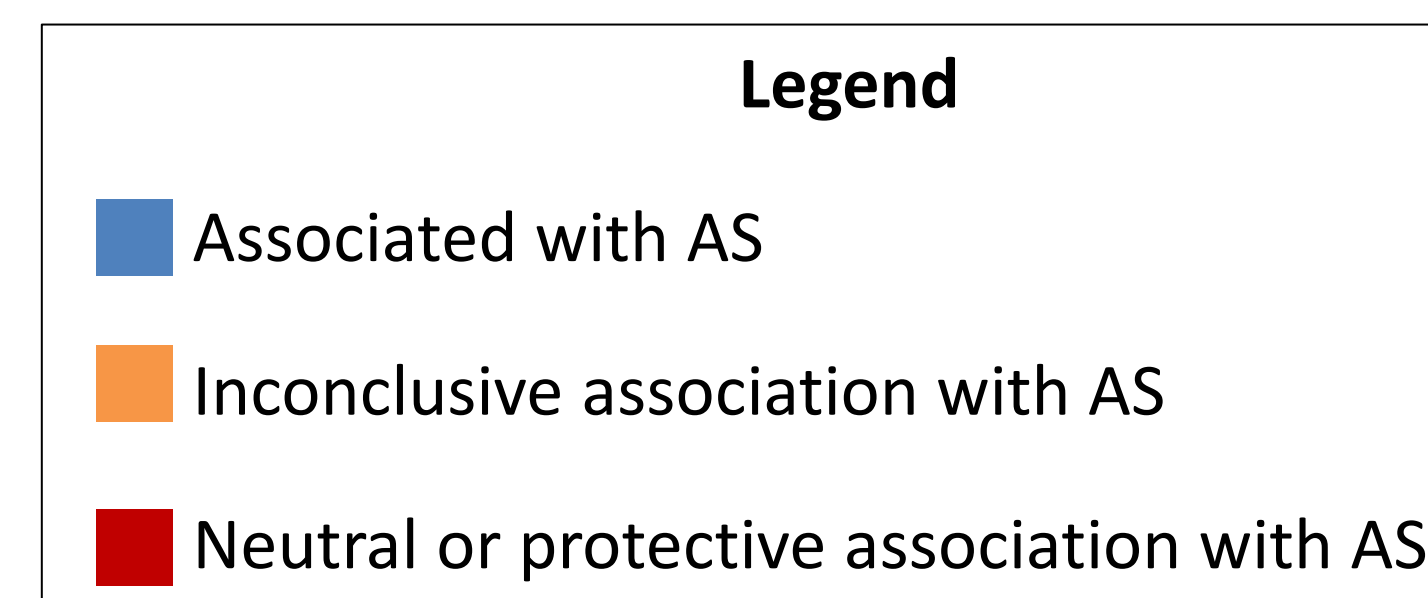
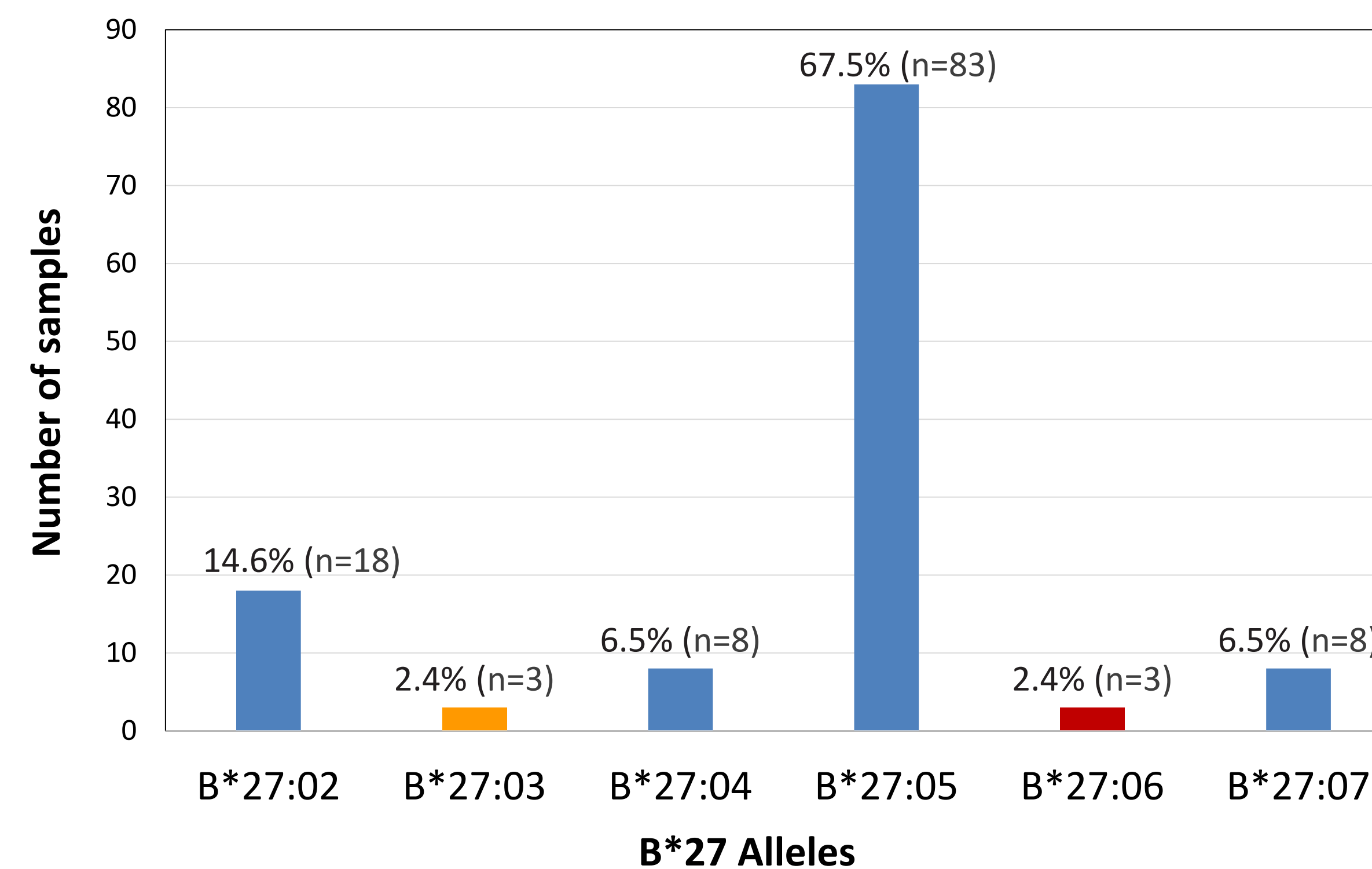


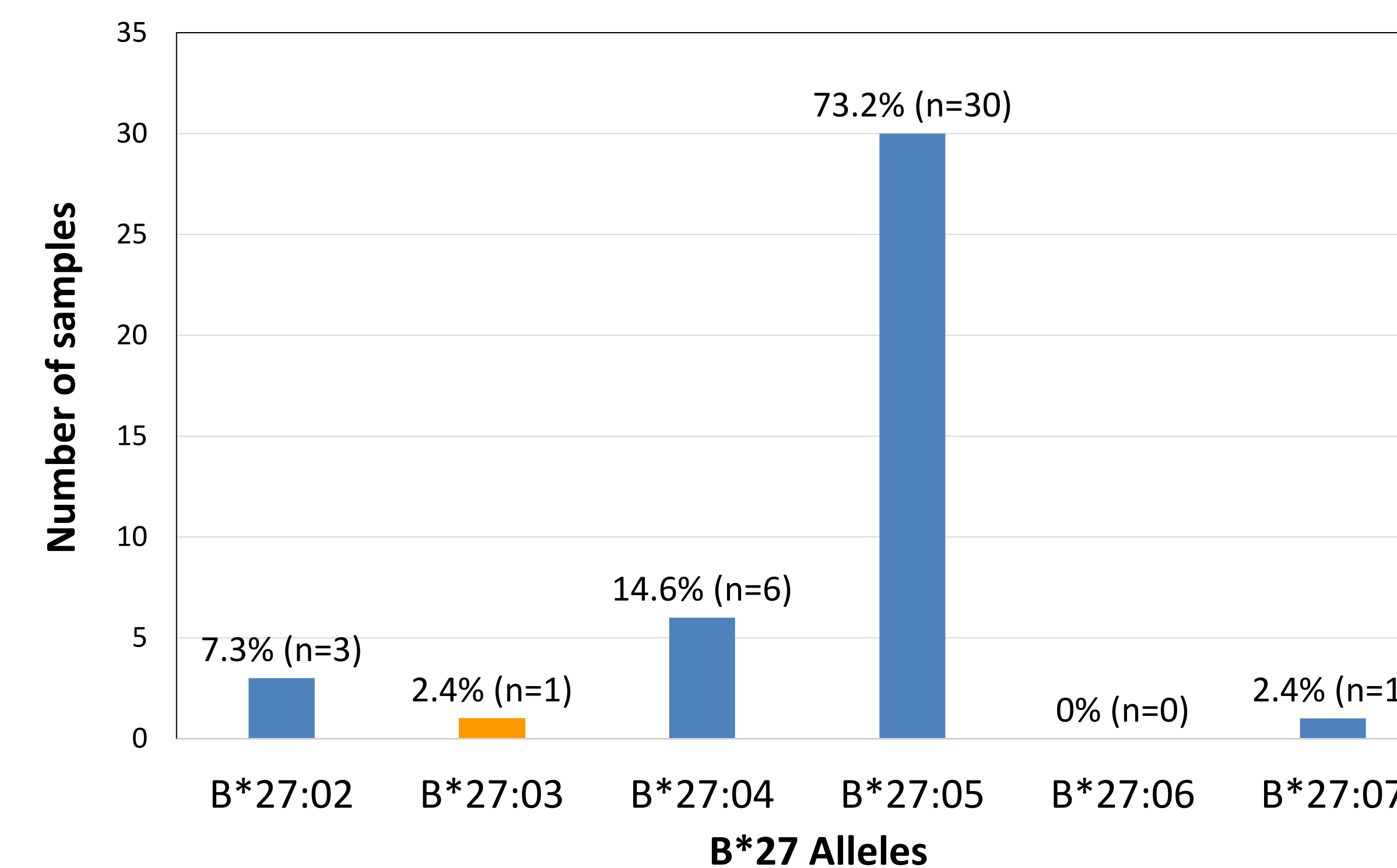
Figure 1. Total number of samples versus distribution of B*27 Alleles



CONCLUSIONS

- B*27:06 was detected, which is 1 of 2 alleles that have not been found to be associated to AS [1]. B*27:03 was detected, which has an inconclusive association with AS.
- Rare B*27 alleles can be detected by NGS and their association with AS is unknown or inconclusive.
- Low resolution HLA typing is sufficient in negative/absent B*27 cases.
- This study demonstrates that although rare, alleles that are not associated with AS are present in the US population.
- When B*27 is positive/present, high resolution typing is warranted to accurately identify HLA-B*27 alleles which are informative for AS disease association and treatment decisions. When reporting B*27 positive alleles, it may be helpful to ensure that clinicians are aware of the allelic differences for B*27 and AS.

Figure 2. Total number of positive samples ordered for B*27 versus distribution of B*27 alleles



REFERENCES

1. Zhu, W., He, X., Cheng, K., Zhang, L., Chen, D., Wang, X., Qiu, G., Cao, X., & Weng, X. (2019). Ankylosing spondylitis: etiology, pathogenesis, and treatments. Bone Research, 7(22). <https://doi.org/10.1038/s41413-019-0057-8>

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