Alliance to leave no-one behind

Italian Conference on AIDS and Antiviral Research
Presidenza del Congresso: A. Antinori, M. Cernuschi, F. Maggiolo, M. Zazzi

Promosso da

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A Machine learning approach to predict Weight change in ART experienced PLWH

Federico Motta has no financial relationships with commercial entities to disclose.

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**Funding:** this study was supported by a grant from Gilead Sciences.
Background

• Contemporary ART has been associated with weight gain (WG)

• We lack a WG definition in terms of:
  • weight or BMI change over time
  • its relationship with metabolic syndrome and other comorbidities

• Machine learning (ML) approaches are suitable to assess P4 medicine (Predictive, Preventive, Personalized & Participatory) and can be used to identify patients at risk of WG

• The objective of this study was to develop ML models able to predict the percentage weight change in each interval of time in ART-experienced PLWH
Methods

• This was an observational study that comprised ART-experienced PLWH attending Modena HIV Metabolic Clinic (MHMC) from 2001 to 2021

• WG was defined as any weight change ≥ 5% at the following annual visit

• 10 progressively parsimonious ML models were trained

• Intelligible explanations were obtained through Shapley Additive exPlanations (SHAP) values, to quantify the contribution of each variable in increasing/decreasing percentage weight change
A total of 3,321 patients generated 18,322 visits valid for the analyses

- 57.6% of our cohort experienced WG at least once
- 16.4% of the visits were about PLWH experiencing WG within the next follow-up

At last follow-up:
- median age was 50 years, 69% were males
- median BMI was 23.4, 6.8% had obesity
- median nadir CD4 was 196 cells/μL, current CD4 was 649 cells/μL
- 94% had undetectable HIV RNA and mean time since HIV diagnosis was 19.9 years

Out of 3,776 observations in the test set, 13.3% about WG; the reference model:
- 367 correctly predicted WG (true positive – TP)
- 6 overestimated WG (false positive – FP)
- 98 underestimated WG (false negative – FN)
- 3,305 correctly predicted non-WG (true negative – TN)
## Results (performance)

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</thead>
<tbody>
<tr>
<td>Sensitivity (recall, true positive rate)</td>
<td>Ability to correctly identify patients with WG who do experience WG</td>
<td>TP / (TP + FN)</td>
<td>75.0%</td>
<td>60.0%</td>
<td>50.0%</td>
<td>50.0%</td>
<td>40.0%</td>
<td>40.0%</td>
<td>40.0%</td>
<td>75.0%</td>
<td>33.3%</td>
<td>60.0%</td>
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<tr>
<td>Specificity (selectivity, true negative rate)</td>
<td>Ability to correctly identify patients without WG who do not experience WG</td>
<td>TN / (FP + TN)</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>96.2%</td>
<td>100%</td>
<td>95.8%</td>
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<tr>
<td>Positive predictive value (precision)</td>
<td>Probability of experiencing WG if the model classifies a patient as “positive”</td>
<td>TP / (TP + FP)</td>
<td>100%</td>
<td>100%</td>
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<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>75.0%</td>
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<tr>
<td>Negative predictive value</td>
<td>Probability of not experiencing WG if the model classifies a patient as “negative”</td>
<td>TN / (FN + TN)</td>
<td>96.3%</td>
<td>92.6%</td>
<td>92.6%</td>
<td>89.3%</td>
<td>89.8%</td>
<td>89.9%</td>
<td>96.2%</td>
<td>87.1%</td>
<td>92.0%</td>
<td></td>
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<tr>
<td>Accuracy</td>
<td>Closeness of the predicted value to an observed value</td>
<td>(TP + TN) / (TP + FN + FP + TN)</td>
<td>96.7%</td>
<td>93.3%</td>
<td>93.1%</td>
<td>90.0%</td>
<td>89.7%</td>
<td>89.7%</td>
<td>93.3%</td>
<td>87.9%</td>
<td>89.7%</td>
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<tr>
<td>$F_\beta=0.5$</td>
<td>Measure of accuracy, considering underestimation errors twice as serious as overestimation ones</td>
<td>$\frac{((1+\beta^2) TP) / ((1+\beta^2)TP + \beta^2 FN + FP)}{}$</td>
<td>93.8%</td>
<td>88.2%</td>
<td>83.3%</td>
<td>83.3%</td>
<td>76.9%</td>
<td>76.9%</td>
<td>76.9%</td>
<td>75.0%</td>
<td>71.4%</td>
<td>71.4%</td>
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<tr>
<td>$F_\beta=1$</td>
<td>Measure of accuracy, considering over/under-estimation errors equally serious</td>
<td>$\frac{((1+\beta^2) TP) / ((1+\beta^2)TP + \beta^2 FN + FP)}{}$</td>
<td>85.7%</td>
<td>75.0%</td>
<td>66.7%</td>
<td>66.7%</td>
<td>57.1%</td>
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<td>75.0%</td>
<td>50.0%</td>
<td>66.7%</td>
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<tr>
<td>ROC AUC</td>
<td>Ability to identify a patient with or without WG with the proposed ML models</td>
<td>$\int TPR , d(FPR)$</td>
<td>87.5%</td>
<td>80.0%</td>
<td>75.0%</td>
<td>75.0%</td>
<td>70.0%</td>
<td>70.0%</td>
<td>70.0%</td>
<td>85.6%</td>
<td>66.7%</td>
<td>77.9%</td>
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<tr>
<td>RMSE</td>
<td>Difference between predicted values and the observed values</td>
<td>$\sqrt{\frac{\sum_{i=1}^{n} (y_i - y_i)^2}{n}}$</td>
<td>4.77</td>
<td>4.05</td>
<td>3.53</td>
<td>4.45</td>
<td>3.71</td>
<td>3.66</td>
<td>3.55</td>
<td>5.35</td>
<td>3.95</td>
<td>5.52</td>
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</table>
Explainability (global SHAP)

Reference Model (N=147)

1) Weight change since last visit (%)
2) BMI
3) Total fat mass (g)
4) Months to future visit
5) Waist circumference
6) Total lean mass (g)
7) IGFBP3
8) Leg fat mass (g)
9) Cumulative exposure to INSTI (months)
10) Current CD8 cell count
97) Switch from TDF to TAF
122) Switch from non INSTI to INSTI without TAF
126) Switch from non INSTI to INSTI with TAF
Explainability (local SHAP)

**Alan**
- **Age (years)** = 55.0
- **Sex** = Male
- **Time to previous visit (months)** = 11.9
- **Weight change at future visit (%)** = higher ⇐ lower
- **BMI** = 24.74
- **Time since HIV diagnosis (years)** = 24.4
- **Weight (kg)** = 79.714

**Bellatrix**
- **Age (years)** = 41.0
- **Time to future visit (months)** = 12.133
- **Weight change at future visit (%)** = higher ⇐ lower
- **BMI** = 28.816
- **Time since HIV diagnosis (years)** = 18.801
- **Weight (kg)** = 71.481

- **Cumulative exposure to INSTI** = 0 (months)
- **Current CD4** = 209 (cells)
- **Waist circumference** = 102 (cm)
- **Hips circumference** = 112 (cm)
- **Cumulative exposure to C** = 0 (months)
- **Weight change since last visit** = -1.0135 (kg)
- **Weight change since last visit** = -14.179 (%)
Conclusions

• The performance metrics allow to choose the best model for each clinical setting/desired prediction:
  • reference model, including body composition assessed with DXA, is the only one ready to be deployed in electronic patient charts at metabolic clinic referral centers
  • parsimonious models, using variables available in standard clinical evaluation settings are insufficient to obtain reliable predictions

• These models confirm the multifactorial nature of WG in which the impact of ART switch/exposure is diluted by the universe of variables contributing to WG
  • major drivers of WG are modifiable risk factors related to lifestyle