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# Progress toward the sustainable development of world cultural heritage sites facing land-cover changes

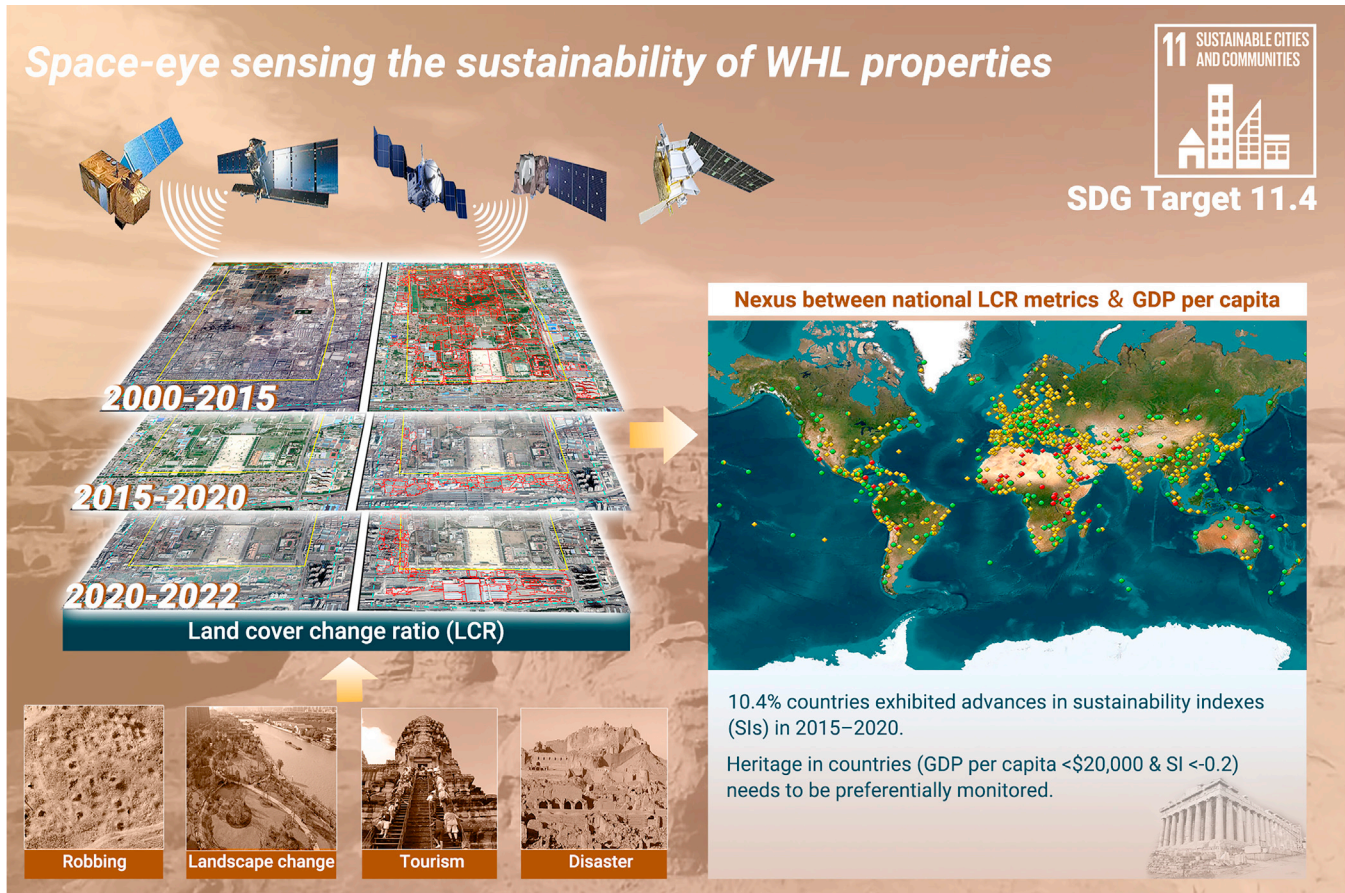
Huadong Guo,<sup>1,3,11</sup> Fulong Chen,<sup>1,2,3,11,\*</sup> Yunwei Tang,<sup>1,2</sup> Yanbin Ding,<sup>4</sup> Min Chen,<sup>5</sup> Wei Zhou,<sup>1,2,3</sup> Meng Zhu,<sup>1,2,3</sup> Sheng Gao,<sup>2</sup> Ruixia Yang,<sup>1,2,3</sup> Wenwu Zheng,<sup>4</sup> Chaoyang Fang,<sup>6</sup> Hui Lin,<sup>6</sup> Ana Pereira Roders,<sup>7</sup> Francesca Cigna,<sup>8</sup> Deodato Tapete,<sup>9</sup> and Bing Xu<sup>10</sup>

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## GRAPHICAL ABSTRACT



## PUBLIC SUMMARY

- Land-cover change metrics enable assessing the progress toward Sustainable Development Goal 11.4.
- 10.4% of countries exhibited advances in sustainability indexes (SIs) in 2015–2020.
- Heritage in developing countries (SI < -0.2) needs to be preferentially monitored.
- Sustainable heritage conservation urges addressing impacts due to land-cover changes.



# Progress toward the sustainable development of world cultural heritage sites facing land-cover changes

Huadong Guo,<sup>1,3,11</sup> Fulong Chen,<sup>1,2,3,11,\*</sup> Yunwei Tang,<sup>1,2</sup> Yanbin Ding,<sup>4</sup> Min Chen,<sup>5</sup> Wei Zhou,<sup>1,2,3</sup> Meng Zhu,<sup>1,2,3</sup> Sheng Gao,<sup>2</sup> Ruixia Yang,<sup>1,2,3</sup> Wenwu Zheng,<sup>4</sup> Chaoyang Fang,<sup>6</sup> Hui Lin,<sup>6</sup> Ana Pereira Roders,<sup>7</sup> Francesca Cigna,<sup>8</sup> Deodato Tapete,<sup>9</sup> and Bing Xu<sup>10</sup>

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The quantification of the extent and dynamics of land-use changes is a key metric employed to assess the progress toward several Sustainable Development Goals (SDGs) that form part of the United Nations 2030 Sustainable Development Agenda. In terms of anthropogenic factors threatening the conservation of heritage properties, such a metric aids in the assessment of achievements toward heritage sustainability solving the problem of insufficient data availability. Therefore, in this study, 589 cultural World Heritage List (WHL) properties from 115 countries were analyzed, encompassing globally distributed and statistically significant samples of “monuments and groups of buildings” (73.2%), “sites” (19.3%), and “cultural landscapes” (7.5%). Land-cover changes in the WHL properties between 2015 and 2020 were automatically extracted from big data collections of high-resolution satellite imagery accessed via Google Earth Engine using intelligent remote sensing classification. Sustainability indexes (SIs) were estimated for the protection zones of each property, and the results were employed, for the first time, to assess the progress of each country toward SDG Target 11.4. Despite the apparent advances in SIs (10.4%), most countries either exhibited steady (20.0%) or declining (69.6%) SIs due to limited cultural investigations and enhanced negative anthropogenic disturbances. This study confirms that land-cover changes are among serious threats for heritage conservation, with heritage in some countries wherein the need to address this threat is most crucial, and the proposed spatiotemporal monitoring approach is recommended.

## INTRODUCTION

Approximately three-quarters of the Earth's land-cover has been modified by humans during the last millennium.<sup>1</sup> Therefore, quantifying the dynamics of land-use/land-cover changes is critical to the Sustainable Development Goals (SDGs) of the United Nations (UN) 2030 Agenda. This is particularly true for Target 11.4, namely, to “strengthen efforts to protect and safeguard the world's cultural and natural heritage” as part of the efforts to make cities and human settlements inclusive, safe, resilient, and sustainable.

In addition to the unavoidable impacts from natural disasters, anthropogenic factors can pose a threat to heritage properties. Such factors include urban development, land conversion, infrastructure projects, and all actions causing irreversible changes to the physical and aesthetic characteristics of the environment where a property (cultural or natural) is located. Notably, these anthropogenic processes have been recognized among the 14 primary factors potentially affecting the outstanding universal value (OUV) of the World Heritage List (WHL) properties of which the UN Educational, Scientific and Cultural Organization (UNESCO) World Heritage Convention (WHC) promotes preservation.<sup>2</sup> The impacts of such anthropogenic factors are not negligible and can either place a property on the List of World Heritage in Danger<sup>3,4</sup> or get it removed from the WHL.<sup>5</sup>

Although total expenditure per capita (TEPC) has been recognized by UNESCO as an internationally comparable indicator<sup>6</sup> (SDG Indicator 11.4.1, “total per capita expenditure on the preservation, protection, and conservation of all cultural and natural heritage”), until 2020, fewer than 30 countries were able to fully or partially calculate this indicator due to a lack of data.<sup>7</sup> Thus, scholars have attempted to determine more versatile indicators that can address the renowned lack of census data and facilitate quantitative and scientific monitoring.<sup>8,9</sup>

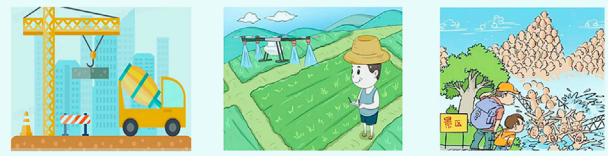
Earth observation (EO) techniques act as an objective and reliable data source to track land-cover changes over long periods of time<sup>10–13</sup> and are currently applied to address SDG targets 11.3<sup>14</sup> and 15.3.<sup>15</sup> Previous studies demonstrated the applicability of EO in assessing the risks to cultural heritage due to man-made hazards, namely, armed conflicts or terrorism,<sup>16</sup> thereby evaluating the progress toward the coupled SDGs<sup>17</sup> and specific targets.<sup>18</sup> Multitemporal remote sensing (RS) images have been proven as effective in generating up-to-date geoinformation on urban settlements at the global scale, particularly when combined with widely automated methods of big data processing and intelligent image analysis.<sup>19–21</sup> While the state of conservation of natural WHL properties has been regularly assessed, for example, using the International Union for Conservation of Nature (IUCN) World Heritage Outlook,<sup>22</sup> cultural WHL properties have typically been monitored on an individual level.<sup>23–26</sup> The few exceptions that exist at the regional and global levels<sup>27</sup> have been evaluated manually. However, such manual approaches are time consuming and thus quickly outdated, or they are unable to satisfy the demand for rapid surveillance, an essential requirement for cultural WHL properties.

In order to address this gap, we propose a solution that exploits EO data to assess the progress toward the sustainable development of WHL properties facing challenges from frequent natural disasters and enhanced anthropogenic activities within the framework of Target 11.4. The proposed approach integrates indicator metrics, data mining, and modeling (Figure 1). Large high-resolution (generally better than 1 m) satellite imagery collections of locations across the globe, publicly available with the Google Earth Engine (GEE), were employed for the analysis. We digitized the core area and buffer zones (both belonging to the protection zones) of the selected cultural WHL properties based on the official inscription documentation of each property available on the UNESCO WHC website. Furthermore, we applied the land-cover change ratio (LCR) by integrating artificial intelligence (AI)<sup>28,29</sup> with the RS big data to evaluate the disturbance status of WHL properties due to either natural disasters or anthropogenic activity. These disturbance metrics were analyzed by adopting the gross domestic product (GDP) per capita (a socioeconomic proxy for the TEPC) and gross national income (GNI) per capita to validate the plausibility of SDG Indicator 11.4.1. As an essential part of the UN 2030 agenda, we propose the use of sustainability indexes (SIs) and percentile SI scores to quantitatively assess each country for its achievement toward SDG Target 11.4 in terms of efforts to manage land-cover-related threats.

Natural disasters



Anthropogenic disturbances



Adopted SDG Target 11.4 for the progress assessment of WHL property sustainability



Earth observations & emerging technologies for the monitoring & quantification



Multi-source satellite images available via GEE



AI and Big data for knowledge discovery

**Procedures:**

1. Boundary digitalization	Shapefiles of core & buffer zones for per WHL property
2. Grouping of WHL properties	WHL properties grouped into three categories of MB, ST, and CL
3. Land cover change ratio (LCR) calculation & mapping	Changes detected by remotely sensed images for calculating LCR indicators
4. Global LCR patterns & socioeconomic development	Exploitation the linkage between measured LCRs & social developmental trajectories
5. Sustainability index (SI) calculation 6. National SI metrics for the SDG target 11.4 progress assessment	SI calculation for WHL properties & their hosting countries (regions) to assess the progress toward SDGs

**Figure 1. Conceptual sketch outlining the methodological workflow by exploiting EO and emerging digital technologies to characterize progress toward SDG Target 11.4 in terms of efforts to manage land-cover related challenges and threats** The combined disturbances to cultural WHL properties originating from natural disasters and anthropogenic activities were estimated via the proposed solution integrating WHL boundary digitization, WHL category grouping, LCR calculation and mapping, global LCR patterns and socioeconomic development, SI calculations, and linkage modeling between national SI and GDP per capita for the progress assessment of SDG Target 11.4.

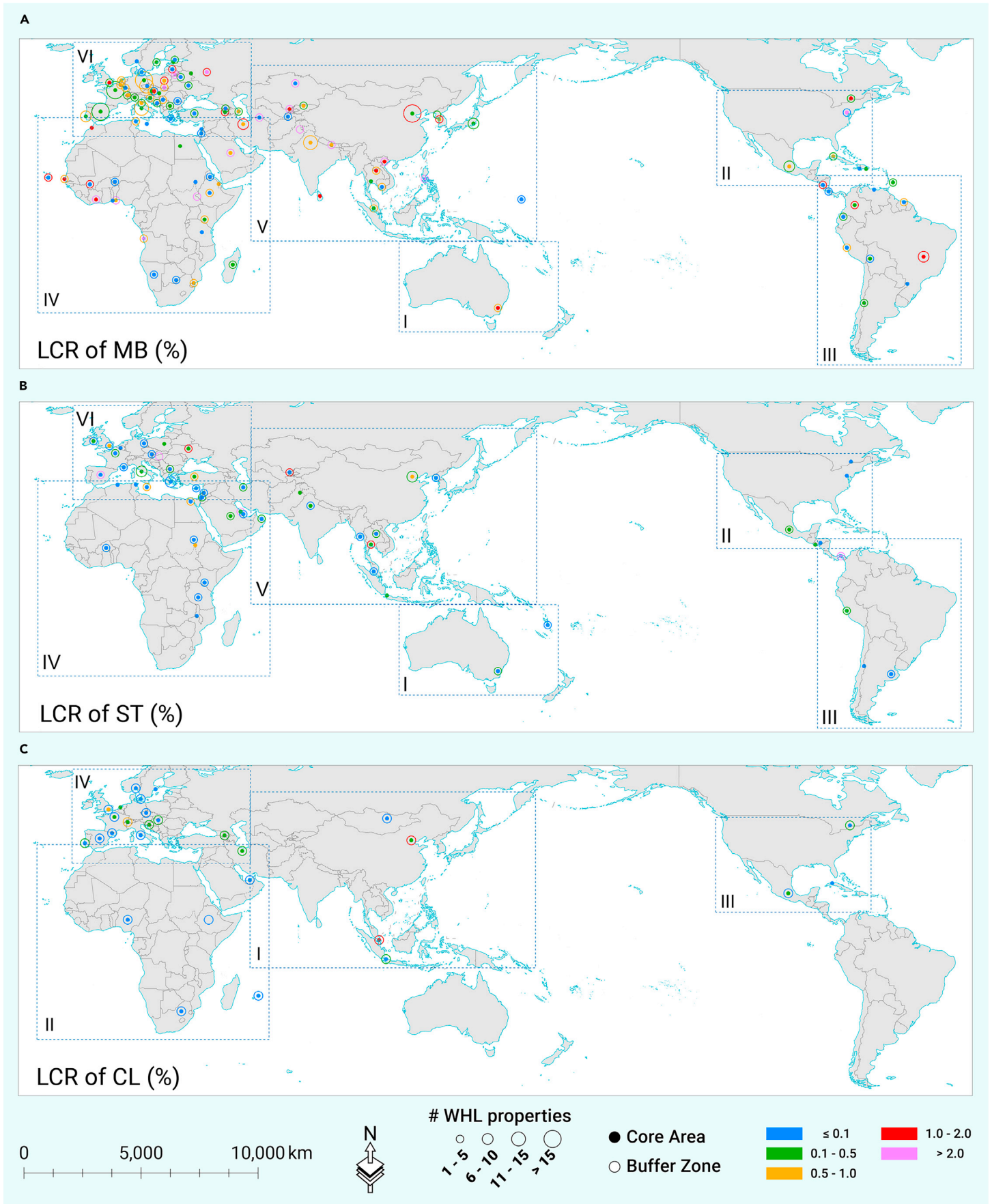
**RESULTS**

**Global LCR patterns**

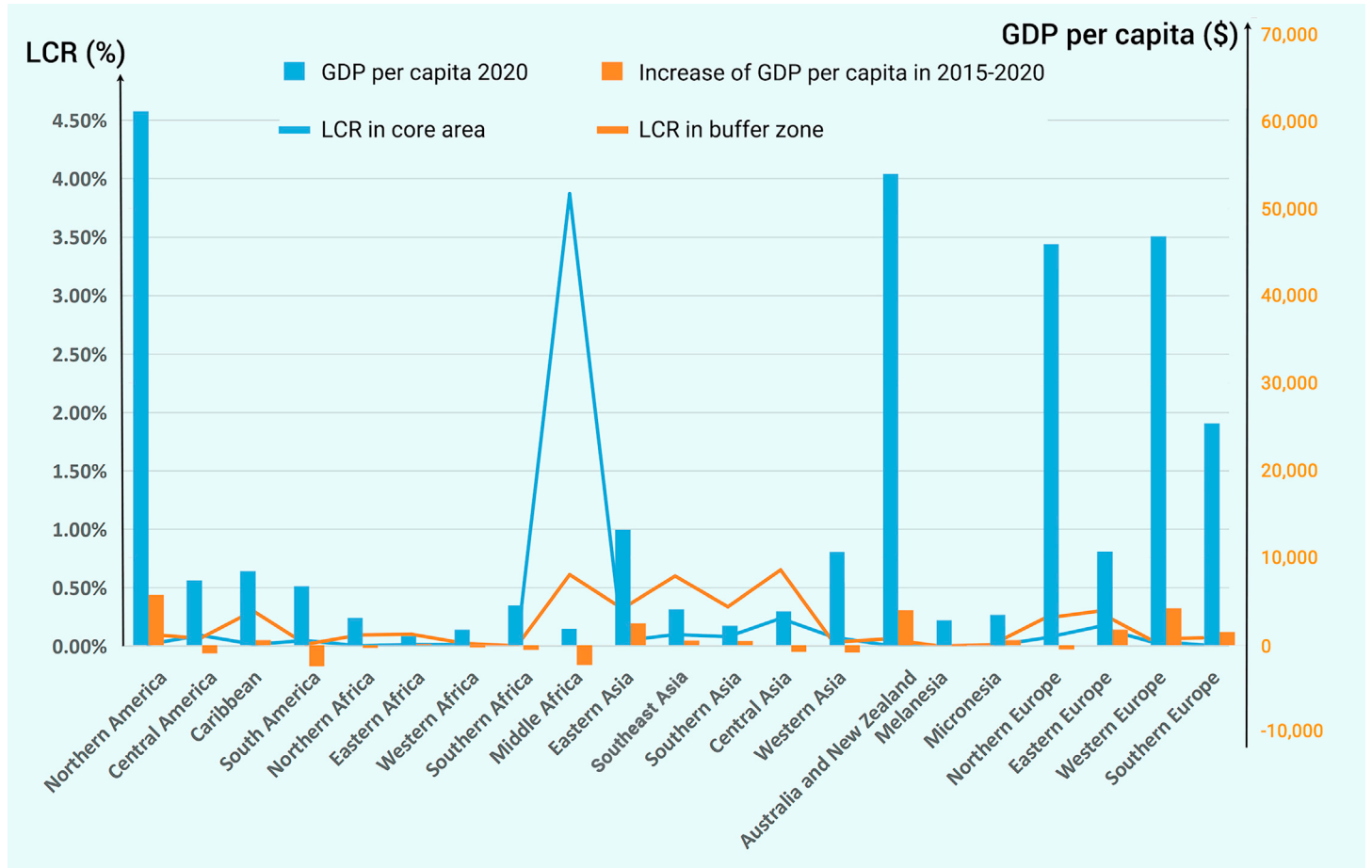
Referring to the UNESCO WHC<sup>30</sup> and corresponding WHC Operational Guidelines,<sup>31</sup> the 589 cultural WHL properties were classified as follows (Table S1): 431 (73.2%) “monuments and groups of buildings” (MB); 114 (19.3%) “sites” (ST); and 44 (7.5%) “cultural landscapes” (CL). Boundary maps and bitemporal high-resolution RS images (Table S2), the majority of which with a spatial resolution better than 1 m, were available for each WHL property to detect changed land-cover patches with a precision of 10 m<sup>2</sup>.

LCR values were statistically estimated per property and country (region). Figure S1 presents the trajectory of land-cover changes occurring between 1969 and 2022 in the protection zones of Daming Palace located in Chang’an City of the Tang Dynasty. This representative site along “The Silk Roads, the Routes

Network of Chang’an-Tianshan Corridor” (inscribed on the WHL in 2014) has withstood various disturbances across time. The spatiotemporal LCR measurements quantitatively depict disturbances threatening the sustainability of the cultural WHL properties. For example, the urbanization occupation of the site in Figure S1 is apparent due to the lack of management during 1969–2000, with LCR values for the core area and buffer zone determined as 20.7% and 24.0%, respectively. From 2000 to 2015, significant environmental remediation measures were implemented following the construction of the National Archaeological Site Park and the inscription on the WHL. Although evident LCRs were observed in this period (74.2% and 29.9% for the core area and buffer zone, respectively), the cultural landscape elements transformed into heritage parks are favorable for the sustainable conservation of this WHL property. Anthropogenic disturbances are estimated to be low in the foreseeable future, as indicated by the measured



**Figure 2.** Spatial patterns of the estimated national LCRs in the core areas and buffer zones per cultural WHL category: (A) MB, (B) ST, and (C) CL MB properties exhibit higher national LCR values attributed to the enhanced and more frequent anthropogenic activities occurring in cities and urban locations.



**Figure 3. Correlation among the LCR values, GDP per capita, and corresponding periodical increase from 2015 to 2020 for the 21 geographic regions** Polynesia and Antarctica are not presented due a lack of LCR estimations. High LCR values generally coincide with middle-income areas rather than regions with a notable periodical increase in GDP per capita, particularly for Central Africa, Southeast Asia, and Central Asia.

LCR values of 1.0% and 2.1% for the core area during 2015–2020 and 2020–2022, respectively. LCRs for the buffer zone beyond 2015 were caused by residential demolitions and municipal facility constructions. Although the LCR is a single indicator, it plays an important role in characterizing the comprehensive socioeconomic (e.g., the renovation of Xi'an Railway Station) and policy (e.g., National Archaeological Site Park) impacts for heritage sustainability at this WHL property.

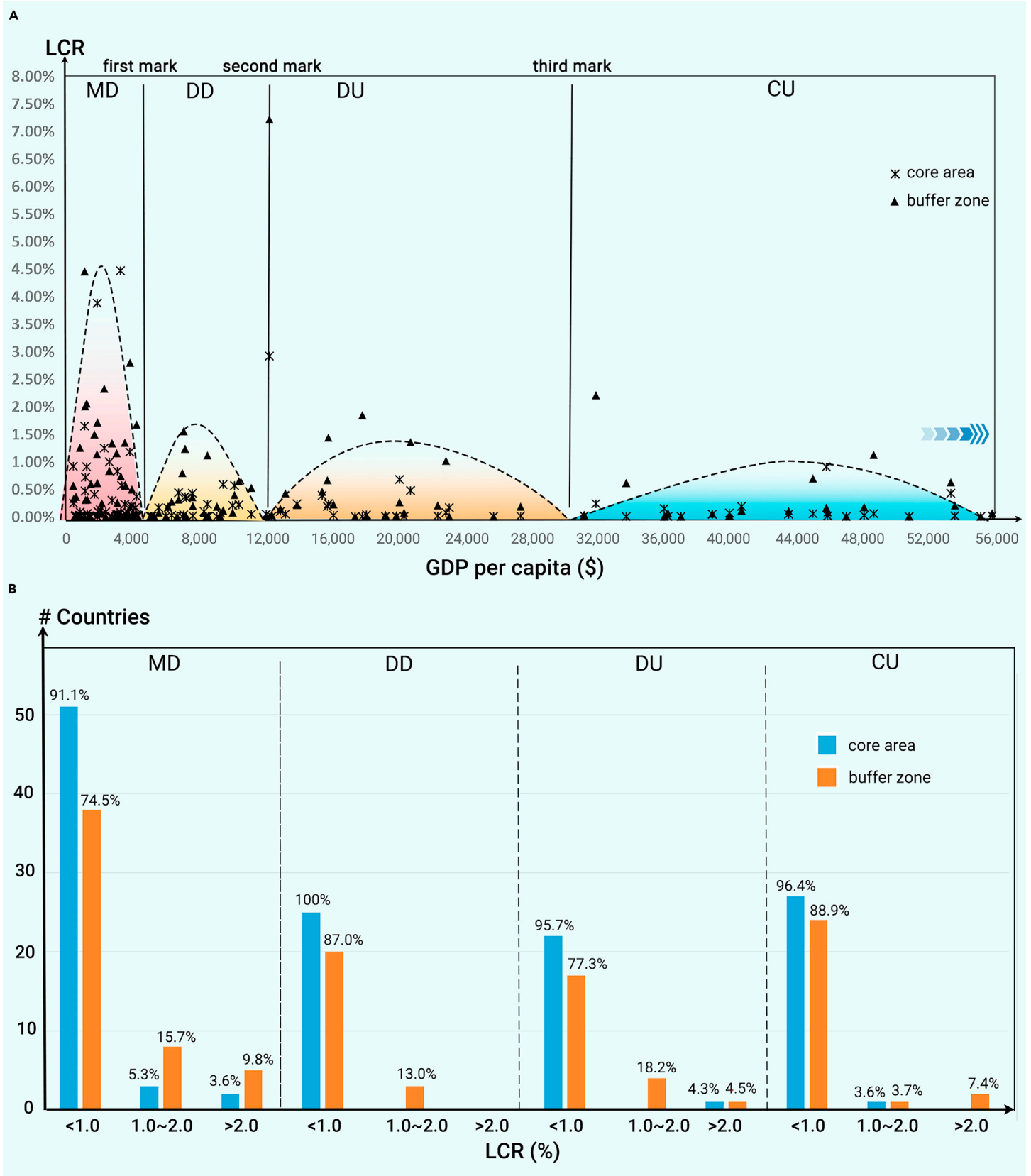
We further exploited the achievements of World Heritage sustainability in the first 5 years since the adoption of the UN 2030 Agenda in 2015. Figures 2 and S2–S4 reveal that the spatial pattern of the three WHL categories vary with the country and continent. In particular, the properties of the MB category generally exhibit higher LCR values compared to those of ST and CL. This is attributed to the typical locations of the MB properties, namely, in cities, urbanized environments, and/or areas inhabited by local communities. Thus, disturbances from anthropogenic activities (dominant factors threatening the heritage sustainability) are more likely to occur in these locations than in rural and remote areas. Moreover, the LCR values in the buffer zones areas are observed to exceed those in the core areas. More specifically, for the core areas, 3%, 6%, 25%, and 66% of LCR values are within the ranges of >1%, 0.5%–1%, 0.1%–0.49%, and <0.1%, while corresponding proportions for the buffer zones are 10%, 12%, 20%, and 58%, respectively. This reflects the more rigorous regulations of WHL properties in the core areas to ensure the conservation of their authenticity and the integrity of the OUV.

Table S3 reports the clustering of the countries under study into 23 geographic regions. No link was identified between the LCR values and the increase in regional GDP per capita between 2015 and 2020. However, Figure 3 reveals an internal correlation between the LCR metrics and GDP per capita in 2020 (note that Polynesia and Antarctica are not presented due to a lack of LCR measurements). This is particularly true in the buffer zones.

The results indicate GDP per capita, the prominent socioeconomic proxy for community well-being,<sup>32</sup> as a potential trigger for land-cover disturbances in WHL properties (i.e., LCR >0.3% at the regional scale), especially for the geographic regions of Central Africa, Southeast Asia, and Central Asia (LCR >0.6%), where the number of middle-income countries (GNI per capita = \$1,036–\$12,535)<sup>33</sup> is dominant. For example, the buffer zone LCRs of Angola (Central Africa), Thailand (Southeast Asia), and Turkmenistan (Central Asia) are determined as 0.61%, 1.23%, and 1.55%, respectively. However, low LCR values are generally observed in high-income countries (e.g., Germany and France in Western Europe). These countries typically have a high level of urbanization as well as well-developed mechanisms and a strong public consciousness in cultural heritage preservation. Notably, several exceptionally low-income countries (e.g., Ethiopia and Burkina Faso in Eastern and Western Africa, respectively) also exhibit low LCR values due to limited cultural investments.

#### Developmental trajectories

Table S4 and Figure 4 present the developmental trajectories toward cultural WHL property conservation across 115 countries. Table 1 defines the following four primary stages for protecting and safeguarding WHL properties at the national scale: Management Disorder (MD); Development Disturbance (DD); Development & Utilization (DU); and Conservation & Utilization (CU). Cultural WHL properties in countries under the MD stage tended to be unregulated. Apart from the lack of management (i.e., 51/56 = 91.1% countries presenting core area LCRs <1.0%) in these countries, inappropriate behaviors (i.e., occupation of built-up areas) are more frequent and uncontrolled, resulting in high LCR values. More specifically, 5.3% and 3.6% of countries have core area LCRs of 1.0%–2.0% and >2.0%, while corresponding LCRs for buffer zones are 15.7% and 9.8%, respectively. However, as the national GDP per capita increases, more attention is focused on the benefits of WHL properties to improve the life quality of local communities,<sup>34</sup> for example, via the tourism industry.<sup>18</sup>



**Figure 4. Development trajectories showing cultural WHL property conservation across countries** (A) LCR values, particularly from buffer zones, exhibit the four socioeconomic development aggregations of MD, DD, DU, and CU, classified by three intersection marks. A mitigatory trend of LCR disturbance is observed with increasing GDP per capita. (B) LCR statistics at the four socioeconomic development levels.

Despite this, disturbances are still prevalent with the socioeconomic development of WHL properties at the DD stage, with 13.0% countries exhibiting buffer zone LCRs within 1.0%–2.0%. This is particularly true for middle-income coun-

tries that prioritize socioeconomic developments and have a national GDP per capita generally below \$12,000. In high-income countries, however, an increasing prevalence of heritage sustainability is observed at the DU stage, including a

**Table 1.** Definitions of the four conservation stages for protecting and safeguarding WHL properties at the national scale

Conservation stage	GDP per capita threshold/interval (\$)	Definition
Management Disorder, MD (lack of conservation measures and unregulated development)	≤ 5,100	interval below the first intersection mark
Development Disturbance, DD (priority for development with conservation measures lacking)	5,100–12,000	interval between first and second intersection marks; note that \$12,000 is also an approximate socioeconomic threshold to discriminate the middle- and high-income countries up to 2020
Development & Utilization, DU (placing equal focus on development and protection)	12,000–30,000	interval between second and third intersection marks; note that most developed economies produced GDP per capita greater than \$30,000 <sup>40</sup>
Conservation & Utilization, CU (deeply rooted sustainability consciousness and cultural memory in the society)	≥ 30,000	interval larger than the third intersection mark

growing awareness and consciousness of the importance in determining a balance between WHL exploitation and utilization.<sup>35</sup> This finding, in turn, correlates with the greater involvement of officers, managers, and stakeholders to work together toward the improved sustainability of WHL properties. Ultimately, a sustainability consciousness and cultural memory<sup>36</sup> are deeply rooted in the public as the society advances to the CU stage, with the GDP per capita reaching ~\$30,000 and the subsequent impacts on the safeguarding and conservation of WHL properties. For example, 3.6% countries at the CU stage exhibit >1.0% core area LCR values, which is over a 50% reduction from the 8.9% value at the MD stage. Thus, a gradual decline in the LCR disturbance intensity is observed as the GDP per capita increases, highlighted by the dotted arcs and percentage values in Figure 4. This result, gathered through the EO-based assessment of LCR, suggests the plausibility of SDG Indicator 11.4.1, despite the lack of relevant census data preventing the achievement of a timely progress evaluation via traditional methods.

### National SI metrics

The LCR-derived national SI metrics reveal that only 12 countries (10.4%) exhibited positive progress achievement in 2015–2020 (Table S4), all of which were either middle-income (Nigeria, Kazakhstan, Thailand, and Iran [Islamic Rep.]) or high-income (Luxembourg, Austria, Netherlands, San Marino, Italy, Germany, Spain, and the United States of America) countries. In particular, 66.6% of the countries exhibiting positive national SI metrics were from CU societies. A detailed analysis was conducted at the national scale to reveal the motives behind these rankings, as well as the constraints intrinsic to the sample selection. For example, Kazakhstan ranked top in the SI metrics during 2015–2020 (Table S4). This can be attributed to its environmental remediation of the WHL property located at the Mausoleum of Khoja Ahmed Yasawi (Figure S5). However, this was the only WHL property in Kazakhstan available for our assessment, which may have caused an overestimation in the results compared to other countries within our study sample that had more WHL properties available for analysis. Such countries include China, which is among the top-five countries with the largest number of cultural WHL properties and was ranked 45 out of 115 based on the SIs determined from our analysis (Table S4). This finding is generally consistent with the overall performance of the SDG index from the Sustainable Development Report 2021,<sup>37</sup> whereby China ranked 57 out of 165, and it further suggests the vital role of GDP per capita in achieving SDG Target 11.4 regarding cultural heritage preservation, protection, and conservation in synergy with other factors such as improved public awareness<sup>38</sup> and governance.<sup>39</sup> The national SI metrics generally reflect the country-scale conservation of WHL properties in the observation period using the negative or positive land-cover change indicators. A total of 20% countries exhibited steady SI values, implying limited cultural efforts for countries at the MD and DD stages or the adoption of rigorous regulations for World Heritage conservation in CU countries. The majority of countries (69.6%) exhibited declining SIs resulting from the land-cover occupation of built-up areas and farmland in the protection zones of WHL properties.

Polynomial fitting between national SIs and GDP per capita data (the solid-line curve in Figure S6) at the global scale reveals a general improvement in the conservation of WHL properties worldwide. However, parallel to the increasing national GDP per capita, several exceptions are observed along the fitted trend, such as Singapore (Figure S7); this can be attributed to con-

struction encroachments in the buffer zone of the only WHL property analyzed for this country, namely, the Singapore Botanic Gardens. The buffer zone of this WHL property is located in downtown Singapore, and thus improvements to facilitate touristic accessibility and leisure activities are simultaneously observed. Moreover, the polynomial fitting is associated with high uncertainties, particularly for low-income countries. The reason for this is 2-fold: (1) cultural investments are limited and typically generate low LCRs, and (2) unregulated management and uncontrolled inappropriate behaviors result in high LCRs. Hence, in order to accurately exploit their correlations, we modeled a representative national SI using logarithmic functions (with exceptions filtered out) (Table S5) and GDP per capita (dotted line curve in Figure S6). The Pearson's coefficient of determination ( $R^2$ ) of 0.76 reveals the strong performance of the model. A GDP per capita of \$60,000 is identified as a statistical transitional threshold for UNESCO state parties presenting a positive achievement toward SDG Target 11.4. Furthermore, the model indicates that WHL properties of countries with a GDP per capita <\$20,000 and SI <-0.2 (equivalent to LCR >0.6 at the national scale) should be preferentially monitored to mitigate the risk of irreversible deterioration of WHL properties.

### DISCUSSION

The LCR and SI metrics were calculated across China to verify the applicability of the proposed methodology at the provincial (county) scale. The conservation areas, including core areas and buffer zones, of 32 properties (out of 38) with enough data to avoid potential errors due to insufficient samples were then digitized for LCR estimations (Figure S8). Following this, land-cover changes based on WHL properties with LCR >1% were identified (Figure S9). Enhanced LCR values (i.e., >1%) were observed for the MB category (Table S6), again confirming the non-negligible impact of anthropogenic activities for properties located in cities or populated areas. The LCR estimation exhibited a cumulative effect over time. The number of cultural WHL properties with LCR >1% in core areas increased from two to five between 2015–2018 and 2015–2020, while buffer zone LCR values doubled (Table S6). We then estimated the provincial indicator metric across China to evaluate the relationship between this disturbance metric and the growth of GDP per capita in space and time (Table S7). However, no significant correlation was identified between the observation periods, thus agreeing with the global/national findings.

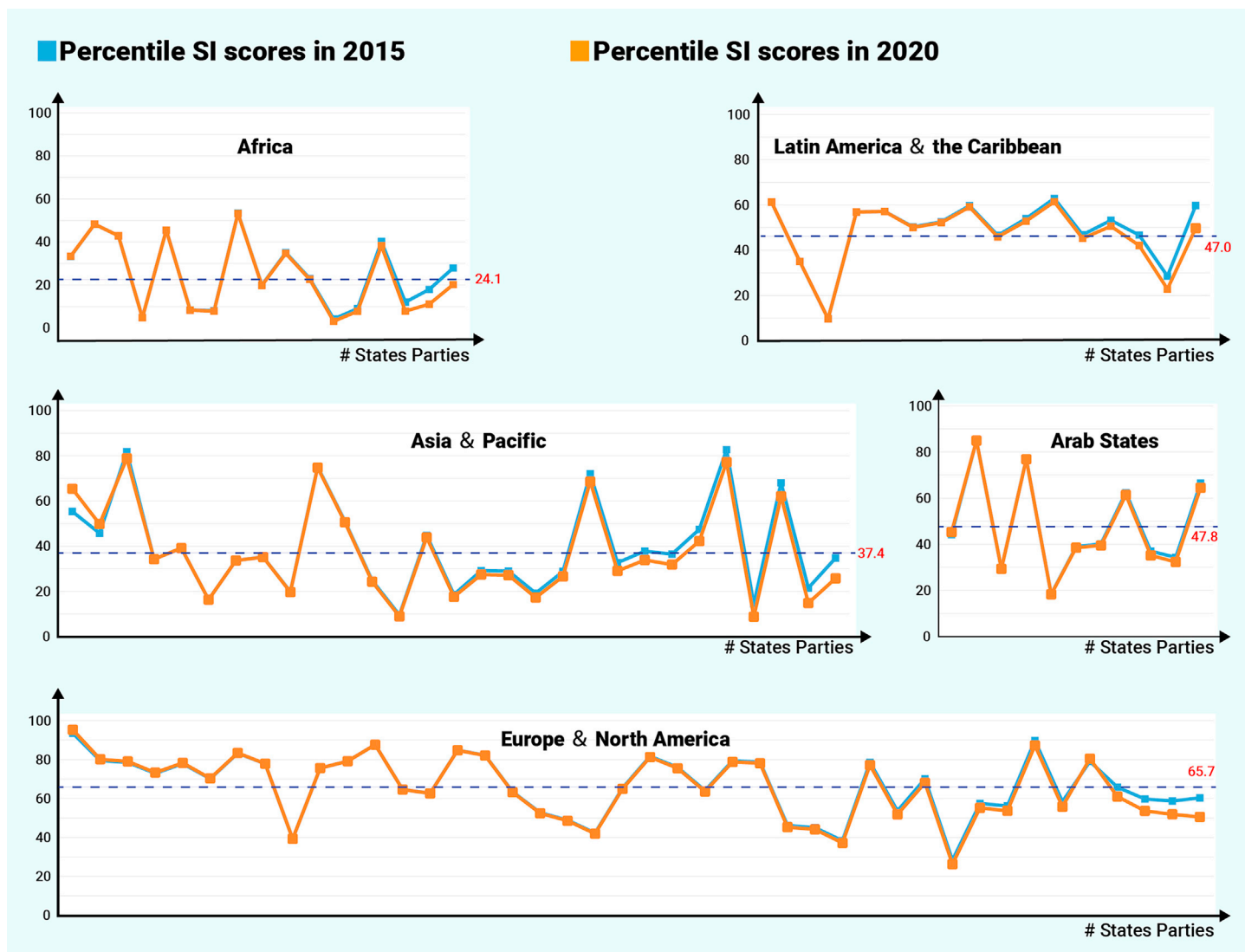
The relative performance of the national SIs exhibits a diverse yet logarithmic fitting trend with the socioeconomic development aggregations (dotted line in Figure S6). We estimated the 2015 percentile benchmark scores for UNESCO state parties following a linear rescaling to the logarithmic fitting function as follows:

$$\text{percentile} - \text{benchmark}_{2015} = 16.46 \ln(\text{GDP per capita}_{2015}) - 96.98$$

where  $\text{percentile} - \text{benchmark}_{2015}$  is the percentile benchmark score estimated for 2015;  $\text{GDP per capita}_{2015}$  is the GDP per capita for 2015; and 16.46 and 96.98 are constants determined from the linear rescaling.

We then periodically updated the national percentile scores by adding the relative SIs or their amplifiers (i.e., a 10-fold applied) to the benchmark scores to assess the national progress toward SDG Target 11.4. Developed countries, such as those in Europe and North America, exhibited the highest average score of 65.7, while developing countries (e.g., African countries) had the lowest average score of 24.1 in 2020 (Figure 5 and Table S4).





**Figure 5. Estimated percentile scores showing the benchmark and updated national-scale SIs for SDG Target 11.4 in 2015 and 2020, respectively, across UNESCO state parties and regions** In order to normalize the index values on a scale of 0–100, a score of 0 is used when the calculated benchmark and updated scores are below zero, and a score of 100 is adopted when the corresponding scores exceed 100. Dotted lines indicate average percentile scores in 2020 across regions.

## CONCLUSION

The results of this study indicate, for the first time, the ability of an analytic model based on LCRs and SIs to effectively assess the progress toward SDG Target 11.4 at the global scale. Moreover, the proposed model has the ability to mitigate the lack of census data and diversity/incompatibility of traditional census approaches across countries. Stochastic anomalies with over-estimations in national SIs can occur owing to the insufficient amount of digitized WHL properties available for national-scale analysis. In addition, uncertainties in the percentile benchmark estimations may exist due to the use of socioeconomic data in the analytic model. However, this study provides a first-hand quantitative assessment of the progress of SDG Target 11.4 for the period 2015–2020. Furthermore, it is possible to constantly improve the SI percentile confidence by updating successive relative national SI estimations up to 2030. The use of EO data, RS technology, and cloud computing ensures that the assessments are replicable, sustainable, and repeatable on an annual basis due to the constant provision of up-to-date satellite images in GEE. This study suggests that more protection and safeguarding efforts should be implemented, particularly for countries falling in the MD–DU conservation stages. Future work will focus on further developing this study by improving the automatic identification of negative/positive land-cover changes and the data-driven model for the accurate estimation of 2015 percentile benchmark scores as well as the assessment of additional SDG targets relevant to land-cover changes.<sup>41</sup>

## MATERIALS AND METHODS

See supplemental information for details.

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## AUTHOR CONTRIBUTIONS

H.G. and F.Chen conceived the research idea. F.Chen and H.G. designed the study. H.G., F.Chen, Y.T., Y.D., M.C., W.Zhou, M.Z., S.G., R.Y., W.Zheng, C.F., and H.L. analyzed data. F.Chen, Y.T., A.P.R., F.Cigna, D.T., and B.X. wrote the paper.

## DECLARATION OF INTERESTS

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. The views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of their institutions.

## SUPPLEMENTAL INFORMATION

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