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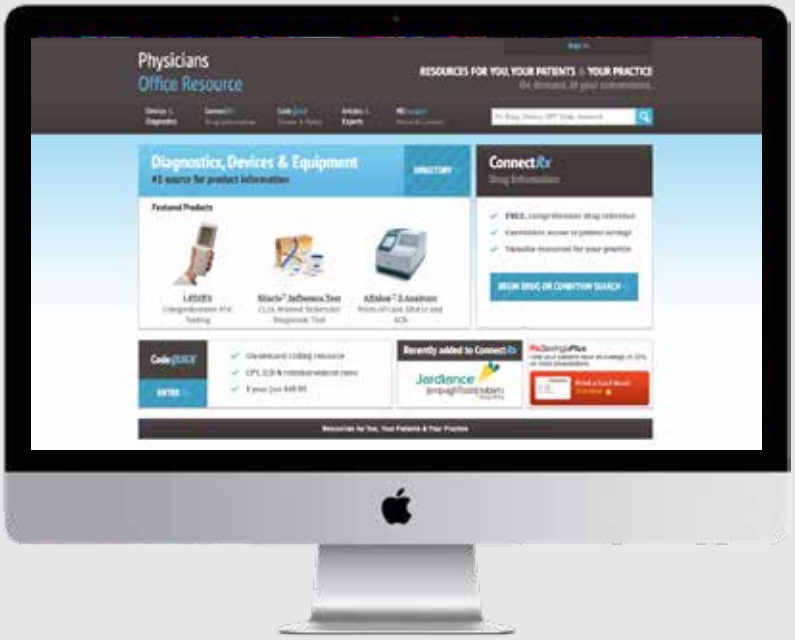
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Medical Education Resources, LLC

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RESTORING THE BRAIN'S BALANCE:

How Nanoparticles May Revolutionize Alzheimer's Treatment

Alzheimer's disease (AD) is a progressive neurodegenerative disorder that is the most common cause of dementia, accounting for an estimated 60–70% of dementia cases globally.

It is characterized by gradual decline in memory, thinking, language, and behavior, eventually interfering with daily life and independence.

On a microscopic level, Alzheimer's is associated with two hallmark pathological features in the brain:

1. **Amyloid plaques** — extracellular deposits of aggregated forms of the amyloid-β protein (Aβ).

2. **Neurofibrillary tangles** — intracellular aggregates of hyperphosphorylated tau protein.

These lesions are thought to contribute to neuronal dysfunction and ultimately neuron death, synaptic loss, and brain atrophy (shrinkage), particularly in brain regions involved in memory such as the hippocampus and cerebral cortex.

The disease is progressive, often beginning years (or even decades) before symptoms appear. Some brain changes (e.g. amyloid accumulation) may start long before overt cognitive decline is evident.

There is no known cure. Currently approved treatments aim to relieve symptoms or slow decline, but none fully reverse or halt the disease.

Risk Factors and Epidemiology

Age
Age is the strongest known risk factor. The likelihood of developing Alzheimer's increases with advancing age (especially past 65).

However, Alzheimer's is not simply "normal aging." Many people age without developing Alzheimer's. *CDC+1*

There is also **younger-onset Alzheimer's** ("early-onset"), which occurs before age 65. Though less common, it can begin as early as in one's 40s or 50s.

Genetics & Family History
A family history of Alzheimer's increases risk, though the genetics are complex and not fully understood.

One of the better-understood genetic risk factors is the *APOE* (apolipoprotein E) gene. The **APOE ε4** allele increases Alzheimer's risk (especially when two copies are present), though not everyone with ε4 develops the disease.

In rare familial (dominantly inherited) Alzheimer's disease, specific mutations (e.g. in APP, PSEN1/2 genes) can lead to early-onset disease in a predictable manner.

Other Risk Factors & Contributing Factors
While the exact triggers for Alzheimer's remain uncertain, researchers have identified a number of contributing factors:

- *Cardiovascular health:* hypertension, high cholesterol, diabetes, obesity, and other cardiovascular risk factors are associated with higher Alzheimer's risk.
- *Head trauma:* moderate to severe head injuries may elevate risk.
- *Lifestyle factors:* physical inactivity, smoking, low mental and social engagement are potential modulators (though causal relationships are challenging to prove).
- O*ther comorbidities:* vascular and cerebrovascular disease, chronic inflammation, and metabolic factors may play roles in disease onset or progression.

Prevalence & Public Health Impact
In the United States alone, over 6 million people aged 65+ live with Alzheimer's disease.

Worldwide, tens of millions suffer from dementia, with Alzheimer's being the most common cause.

Given rising lifespans globally, Alzheimer's poses a growing public health and social challenge — not only in terms of medical care costs, but also the burden on caregivers and families.

Symptoms & Clinical Course

Early Signs
- Mild memory lapses: forgetting recent conversations, appointments, or names.
- Difficulty with planning, problem-solving, organizing tasks
- Misplacing objects, difficulties in spatial orientation
- Changes in mood, personality, or social withdrawal

At first, individuals may be aware of their difficulties; companions or families may notice the deficits later on.

Progressive Decline
As the disease advances:
- Memory loss intensifies: forgetting events, names, faces
- Language difficulties: trouble finding words or following conversations
- Impaired judgment and decision-making
- Problems with visuospatial skills (e.g. driving, navigating)
- Behavioral and psychiatric symptoms: agitation, apathy, delusions, depression
- In late stages: inability to carry on conversation, loss of basic self-care abilities, requiring full dependence

On average, after diagnosis, life expectancy is about 4 to 8 years, though many live longer (up to 15–20 years) depending on age, health status, and comorbidities.

Current & Emerging Approaches to Treatment
Because Alzheimer's is a complex, multifactorial disease, therapeutic strategies take multiple forms: symptomatic treatments, disease-modifying therapies, and experimental directions.

Symptomatic Treatments (Approved Therapies)
These therapies do *not* cure Alzheimer's but aim to ease symptoms or slow decline:

- **Cholinesterase inhibitors** (e.g. donepezil, rivastigmine, galantamine): aim to increase levels of acetylcholine (a neurotransmitter reduced in Alzheimer's) and help cognition or behavior in mild-to-moderate stages.
- **Memantine:** targets the glutamatergic (NMDA receptor) system and may help in moderate-to-severe stages.

These treatments typically yield modest symptomatic benefit and do not substantially halt disease progression.

Disease-Modifying Therapies (Targeting Pathology)
The more ambitious goal is to slow, halt, or reverse underlying disease processes (amyloid, tau, inflammation, neuroprotection). Some of the strategies being explored include:

- **Anti-amyloid antibody therapies**: such as aducanumab (Aduhelm), lecanemab (Leqembi), and donanemab (Kisunla), which target various forms of amyloid-β to reduce its accumulation or promote clearance.
  - · Lecanemab has shown in clinical trials a slowing of cognitive decline in early-stage Alzheimer's.
  - · These therapies sometimes carry risks such as brain swelling or microhemorrhages (so-called ARIA: amyloid-related imaging abnormalities).

- **Anti-tau therapeutics:** targeting tau aggregation, phosphorylation, or spreading of tau pathology (e.g. tau antibodies, small molecules). This is a more challenging area, still mostly in research phases.

- **Anti-inflammatory and immune-modulating approaches:** given the role of neuroinflammation and microglia in Alzheimer's, therapies that regulate microglial activity or chronic inflammation are under investigation.

- **Neuroprotection and regenerative strategies:** promoting neuron survival, synaptic resilience, or even neural regeneration.

- **Small molecules, peptides, and gene therapies:** designed to intervene in disease pathways (oxidative stress, mitochondrial dysfunction, protein homeostasis)

- **Early detection & biomarker approaches:** using imaging (PET scans), cerebrospinal fluid biomarkers, and (more recently) blood-based biomarkers to detect Alzheimer's before symptoms arise and enable earlier intervention.

- **Nanotechnology / nanomedicine:** using nanoparticles to deliver drugs across the blood-brain barrier, to target amyloid or tau, or to act as catalytic agents or "nanozymes" to degrade pathological proteins.

Because Alzheimer's is slowly progressive and begins long before symptoms, many believe that effective therapies will need to be applied early — possibly before cognitive deficits are overt.

Challenges & Outlook

- The **blood-brain barrier (BBB)** is a major obstacle for drug delivery to the central nervous system. Many therapeutic molecules cannot cross it efficiently.

- Many past therapies that showed promise in animal or cellular models have failed in human trials, due to complexity of human brain biology.

- Side effects and safety are important risks (e.g., brain swelling, bleeding in anti-amyloid therapies).

- Alzheimer's is biologically heterogeneous; different patients may respond variably to therapy.

- Early diagnosis and intervention are crucial; by the time symptoms are severe, much neuronal damage may already be irreversible.

Nevertheless, the pace of Alzheimer's research has accelerated, with increased funding, better biomarker tools, and novel interdisciplinary approaches (including nanotechnology) offering hope.

Nanoparticles to Clear Brain Plaque: The Recent Mouse Study
A recent study (reported by UPI and other outlets) describes how scientists used specially designed nanoparticles to promote clearance of Alzheimer's-associated toxins (notably amyloid-β) in mouse models. Below is a summary of their approach and findings.

Core Concept & Rationale

- The researchers' focus was not only on targeting amyloid-β directly, but on repairing the brain's **blood-brain barrier (BBB)** and supporting the cerebrovascular system's natural clearance pathways.

- They used **supramolecular nanoparticles** that act not merely as passive drug carriers but as active **biofunctional agents** — meaning the nanoparticles themselves exert therapeutic actions.

- The idea is that by restoring vascular and barrier health, the brain's innate "waste disposal" systems (e.g. transporters, perivascular clearance) can resume removing amyloid-β and other toxic species more effectively.

Experimental Approach

- The nanoparticles were administered to Alzheimer's model mice (presumably via systemic injection, likely bloodstream).

- The researchers assessed amyloid-β levels, blood-brain barrier integrity, and cognitive/behavioral outcomes in the treated mice over time.

- Their design allowed the nanoparticles to promote repair and normalization of cerebrovascular function and barrier integrity, rather than focusing exclusively on amyloid binding or clearance.

Key Findings & Outcomes

- Within **one hour** of nanoparticle administration, the treated mice displayed a **50–60% reduction** in amyloid-β levels compared to controls.

- Over extended treatment, the mice exhibited **striking reversal of Alzheimer's-like pathology**: improved blood-brain barrier function, restoration of vascular health, and cognitive/behavioral recovery.

- The researchers interpret this as a **feedback mechanism**: once the barrier and vascular function are repaired, the brain's own clearance systems resume, leading to further removal of toxins (like amyloid-β) and restoration of homeostasis.

The authors argue that this vascular-focused approach may be more effective than targeting neurons directly, especially when barrier health is compromised.

Significance and Caveats

- The results are compelling in mice, showing rapid amyloid clearance and functional recovery.
- However, **translating to humans is challenging**. Human brains, blood-brain barriers, and cerebral vasculature are more complex, and many Alzheimer's treatments that succeeded in mice have failed in human clinical trials.
- Safety, dosing, off-target effects, immune responses, and long-term stability are key obstacles that must be addressed in future work.
- Nonetheless, the study highlights an intriguing paradigm shift: focusing on **vascular repair and barrier restoration** as a lever to revive intrinsic clearance pathways — essentially turning the brain's own waste management back on.

Conclusion & Perspective

Alzheimer's disease remains one of the great medical challenges: a slowly progressive, multifaceted neurodegenerative disorder for which there is no cure. Its pathology involves complex interplay of protein aggregates (amyloid and tau), neuronal loss, synaptic dysfunction, vascular compromise, and chronic inflammation.

Emerging therapies aim beyond just symptomatic relief — targeting the root processes of disease. Among these, nanotechnology offers a promising toolkit: nanoparticles that can cross or modulate the blood-brain barrier, carry therapeutic cargo, or act as catalytic agents to neutralize pathological proteins.

The recent mouse study showing that supramolecular nanoparticles can restore cerebrovascular integrity, then trigger rapid amyloid clearance and cognitive recovery, is a provocative proof-of-concept. It suggests that repairing the vascular/BBB system might unlock the brain's own regenerative and clearance mechanisms.

That said, the journey from mouse models to human patients is long and fraught with hurdles. Yet progress in biomarker detection, improved imaging, safer delivery systems, and a deeper understanding of Alzheimer's heterogeneity make me cautiously optimistic that advances like this might pave the way for more effective human therapies in the future.

If you like, I can go deeper into the types of nanoparticles used, the mechanism by which they restore the BBB, or review other recent nanoparticle-based Alzheimer's studies. Would you like me to dig into those?



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1. Smolderen KG, Ameli O, Chaisson CE, Heath K, Mena-Hurtado C. Peripheral Artery Disease Screening in the Community and 1-Year Mortality, Cardiovascular Events, and Adverse Limb Events, AJPM Focus (2022), https://doi.org/10.1016/j.focus.2022.100016



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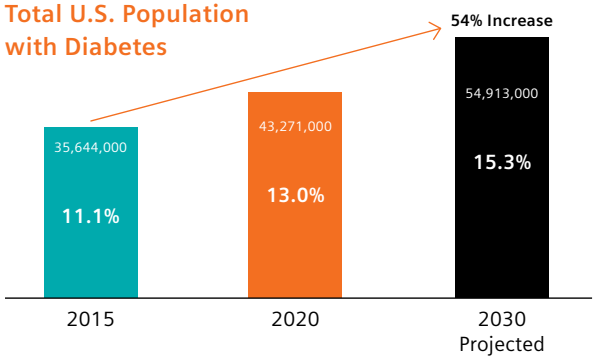
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1. Rowley, William R et al. "Diabetes 2030: Insights from Yesterday, Today, and Future Trends." Population health management vol. 20,1 (2017): 6-12. doi:10.1089/pop.2015.0181.

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Artificial Intelligence in Diabetes Care:

EVOLVING ROLES FOR THE PRIMARY CARE PHYSICIAN

BY ADAM IRVINE, PHYSICIANS OFFICE RESOURCE

Diabetes care has long been a cornerstone of primary care practice. With nearly 38 million Americans living with diabetes and another 98 million with prediabetes, the majority of whom are managed outside of endocrinology settings, primary care physicians sit at the center of diabetes detection, management, and prevention. From early diagnosis and medication initiation to long-term monitoring, education, and coordination of multidisciplinary care, the PCP's role is both broad and deeply personal.

Managing diabetes in primary care, however, is increasingly complex. The modern PCP must juggle medication regimens that have expanded far beyond metformin, keep pace with evolving treatment algorithms, interpret data from continuous glucose monitors (CGMs), and tailor care plans to individual comorbidities, health literacy, and socioeconomic barriers. Add to this the administrative load of electronic health records (EHRs) and limited visit time, and it becomes clear that even the most experienced physicians are stretched thin in their efforts to deliver guideline-based, patient-centered care.

This is where artificial intelligence (AI) is beginning to make a measurable difference. Once viewed as a futuristic concept, AI is now emerging as a practical ally in the primary care setting—augmenting, not replacing, the physician's judgment. From risk prediction and early detection to automated insulin titration, decision support, and patient engagement, AI technologies are transforming how diabetes is identified, treated, and followed up.

For primary care physicians, this transformation is not about ceding control to machines but about leveraging intelligent systems to make care more precise, proactive, and personalized. AI-driven algorithms can flag undiagnosed cases, recommend medication adjustments, identify patients at risk for complications, and provide ongoing behavioral coaching between visits—all while freeing clinicians to focus on the art of medicine: communication, motivation, and empathy.

In this article, we explore how artificial intelligence is reshaping diabetes care across the continuum—from prediction and prevention to treatment optimization and complication monitoring—through the lens of the primary care physician. We will examine where AI tools are already proving their value, what challenges remain, and how thoughtful integration can help PCPs provide higher-quality, more efficient, and more individualized care to their patients with diabetes.

AI for Risk Prediction and Early Detection

One of the earliest and most promising AI roles is in identifying individuals at high risk for incident diabetes or early-stage disease before overt hyperglycemia.

- **Risk models and screening:** ML models can integrate demographic, lab, and electronic health record (EHR) features to generate individualized risk scores for progression to type 2 diabetes. These models may outperform traditional risk calculators by discovering nonlinear interactions and novel predictors.[1,5]
- **Nontraditional signals:** Some investigational AI tools analyze ECG data or imaging biomarkers to detect subtle metabolic signatures that precede biochemical changes. In the U.K., for instance, a trial is planned to test an AI-ECG tool (called Aire-DM) that flags future diabetes risk up to 13 years before onset.[2]
- **Type 1 risk prediction:** Beyond type 2 disease, AI has been used to better identify those at high risk of developing type 1 diabetes in the near term, potentially enabling earlier intervention or enrollment in prevention trials.[3]

Implications for PCPs

By embedding AI-based risk scores in the EHR workflow, PCPs

For PCPs, the optimal approach is one of cautious, phased adoption—beginning with well-validated, lightly disruptive tools—and continuous evaluation.

could better target screening, lifestyle counseling, or structured prevention. For example, patients flagged as high risk might be prioritized for more frequent monitoring, nutritional/behavioral interventions, or inclusion in digital prevention programs.

Subphenotyping and Personalization of Type 2 Diabetes

Not all patients with type 2 diabetes are biologically identical. AI can help uncover subtypes that may predict differential treatment response, complication risks, or disease trajectories.

- **Glycemic trajectory clustering:** Unsupervised ML techniques can group patients by patterns of glucose progression, insulin secretion decline, or comorbidity pro files.
- **Subtype discovery with CGM data:** Researchers at Stanford used AI algorithms on continuous glucose monitor (CGM) datasets to delineate multiple subtypes within type 2 diabetes, offering the possibility of more precise therapeutic choices (e.g., agents with better effect in one subtype versus another).[11]
- **Digital twins / in silico modeling:** Some platforms create a "digital twin" of a patient (a computational model reflecting their physiology and responses), which can simulate how different treatment options might affect glycemic control or metabolic outcomes. Notably, a "Whole-Body Digital Twin" platform showed higher remission rates of type 2 diabetes compared to standard care in a pilot trial.[4]

Implications for PCPs

In practice, such subtyping could guide earlier choices (e.g., use of GLP-1 RA, SGLT2 inhibitors, or insulin) tailored to an individual's predicted trajectory or response, rather than a "one-size-fits-all" escalation.

Clinical Decision Support and Insulin Dosing Algorithms

Perhaps the most clinically actionable AI use is decision support—helping clinicians choose the best interventions and guiding insulin management.

- **Insulin titration and dosing:** Reinforcement learning and predictive modeling have been used to propose dynamic insulin regimens that adapt to glucose trends and patient behavior.[5]
- **AI-based decision support systems (CDSS):** Some systems offer real-time recommendations for dosing adjustments, flagging extreme glucose excursions, or suggesting incremental changes. For inpatients, AI-based systems for insulin titration (e.g., iNCDSS) have been evaluated. A multisite randomized trial in China found that AI-based insulin CDSS was noninferior to endocrinologist-driven management.[6]
- **Integration with closed-loop / AID systems:** In patients on insulin pumps or multiple daily injections with CGM, AI is integral to automated insulin delivery (AID) systems. Neural network–based algorithms (e.g., "neural-net artificial pancreas") have shown improvements in time in range (TIR).[7] [12]

Implications for PCPs

For most PCPs not directly managing insulin pumps or complex regimens, AI CDSS can offer suggestions (e.g., "increase basal insulin by X units," "adjust mealtime ratio") while leaving final judgment to the clinician. The key is to ensure interoperability with the EHR and maintain clarity around alerts and overrides.

Patient Engagement, Education, and Behavioral Nudges

AI is extending beyond clinician-facing tools into direct patient support—an area where primary care often struggles due to limited staff bandwidth.

- **Conversational agents / chatbots:** AI-driven virtual coaches can answer patient questions, deliver diabetes education (nutrition, medication adherence, foot care), and adapt messaging to individual learning styles.[8]
- **Personalized "nudges":** AI can analyze a patient's behavior, glucose patterns, medication adherence, and context to generate customized reminders—e.g., encouraging meal time bolus, increasing activity, or checking glucose. In one study in type 2 diabetes, AI-powered nudges showed promise in improving glycemic outcomes.[9]
- **Lifestyle guidance:** AI models can ingest diet logs, wearable sensor data (e.g., step counts, heart rate), and CGM trends to

deliver actionable suggestions about meal composition, timing, and physical activity patterns.[5] [10]

- **Voice/ambient interfaces:** Researchers are exploring AI via smart speakers to support diabetes self-management—offering reminders, education, or prompts to log glucose values. One Stanford-led trial using an AI-based smart speaker yielded improvements in glycemic control.[11]

Implications for PCPs

By offloading some education and routine follow-up to AI-driven agents, PCPs can focus their time on higher-yield interactions. PCPs will want to vet such tools for accuracy, transparency, and privacy protection before recommending them to patients.

Complication Screening and Prognostication

AI is making inroads into predicting and detecting complications—an area of critical importance in diabetes care.

- **Retinopathy screening:** AI-based evaluation of fundus photos to detect and grade diabetic retinopathy is one of the most mature AI applications. Multiple algorithms have achieved regulatory clearance and are being deployed in screening programs.[12]

- **Predicting nephropathy, neuropathy, and cardiovascular risk:** ML models can forecast the progression of chronic kidney disease, risk of diabetic neuropathy, or macrovascular events by using longitudinal lab values, genomics, and other covariates.[5] [12]

- **Prognostic modeling for hospitalization:** AI might flag patients at imminent risk of decompensation or hyperglycemia-related hospitalization, enabling preemptive intervention.[5]

Implications for PCPs

Incorporation of AI-based complication risk scores into the EHR could sharpen decisions on screening intervals (e.g., when to order microalbuminuria, refer to nephrology, or order retinal imaging) and inform patient discussions about intensity of control.

Implementation Challenges, Risks, and Ethical Concerns

Despite the promise, AI adoption in diabetes care faces substantial challenges. PCPs should be aware of these when evaluating or deploying AI tools.

- **Data bias and representativeness:** Many AI models are trained on datasets that may underrepresent minority populations, lower socioeconomic strata, or specific geographic regions. This can lead to performance drift or unfairness.[12]

- **Overfitting and generalizability:** AI models may perform well on their training dataset but degrade in new settings or with different patient populations.[5]

- **Data integration and workflow friction:** Many AI tools require seamless integration with EHRs, CGM platforms, and clinical systems. Poor UX or lack of interoperability can undermine uptake.[12]

- **Alert fatigue and trust:** Excessive or non-actionable alerts can lead to clinician fatigue or ignoring suggestions. Building clinician trust in AI recommendations (and allowing for override) is essential.[12]

- **Regulation, liability, and oversight:** Clinicians must understand regulatory status (FDA clearance, CE marking) and liability—if following AI guidance leads to patient harm, who is responsible?

- **Explainability and transparency:** "Black box" models may offer limited interpretability. Clinicians may be reluctant to act on opaque recommendations.
- **Patient privacy, data security, and consent:** As AI tools accumulate sensitive data (glucose trends, behavior logs), safeguarding privacy is critical. Informed consent and clear data stewardship policies are needed.

- **Health inequities and access:** AI tools may exacerbate disparities if only available to patients with smartphones, continuous glucose monitors, or digital literacy.[5]

Practical Considerations for PCP Adoption

For PCPs to adopt AI tools meaningfully, a few guiding principles may help:

1. Start with modest pilots
Begin with limited implementation—e.g., offering AI-based patient education to a subset, or using decision support only for complex insulin cases—before scaling.

2. Workflow integration is critical
Tools must fit naturally into EHR-based workflows, minimizing clicks and interruptions. AI outputs should be concise, prioritized, and actionable.

3. Clinician oversight and override
Always preserve clinician final decision-making. AI should suggest, not dictate. Provide mechanisms for clinicians to override or ignore.

4. Validate locally
Monitor tool performance in your own patient population. Compare outcomes (e.g., glycemic control, hypoglycemia) before and after adoption.

5. Educate clinicians and staff
Training, transparency, and clear user guides are essential to build trust and correct misconceptions about AI.

6. Engage patients thoughtfully
Introduce AI-based patient tools gradually, explain to patients their role, benefits, and limitations, and monitor adherence or feedback.

7. Partner with technology / informatics teams
Close collaboration with IT, data governance, and compliance teams ensures smooth integration, security, and maintenance.

Future Horizons

Looking ahead, several trends suggest how AI may further transform primary care–led diabetes management:

- **Generative AI and synthetic data:** Tools that fill gaps in limited data or simulate patient trajectories may support more robust modeling in smaller practices.[13]

- **Federated learning:** Using models trained across distributed data sources (without sharing raw data) can improve generalizability while protecting privacy.[5]
- **Ambient sensing and Internet-of-Things integration:** Smart sensors, wearables, and passive monitoring (e.g., continuous dietary intake logs, physical activity sensors) may feed predictive AI systems without requiring patient input.

- **Adaptive therapy loops:** AI that continually learns from individual patient responses (i.e., closed feedback loops) may refine therapy algorithms over time.

- **Cross-disease modeling:** Because many patients with diabetes have comorbidities (hypertension, CKD, heart disease), AI models that manage multiple conditions in concert may become more common.

- **Population health and risk stratification:** AI could support proactive outreach in primary care panels—flagging patients needing follow-up, intensification, or screening before they fall through the cracks.

The rising maturity and variety of AI applications in diabetes care offer primary care physicians powerful new tools. From early risk prediction and individualized therapy to decision support, patient engagement, and complication detection, AI promises to enhance efficiency, precision, and outcomes. However, realizing this promise demands careful attention to data quality, workflow design, clinician trust, equity, regulation, and implementation strategy.

For PCPs, the optimal approach is one of cautious, phased adoption—beginning with well-validated, lightly disruptive tools—and continuous evaluation. Over time, AI may shift some of the cognitive and analytic burden out of our daily practice, freeing us to focus more on complex judgment, relationship building, patient teaching, and holistic care.

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Patients with Peripheral Artery Disease (PAD) who may be facing a heart attack, stroke, amputation, or even death within the next 5 years.

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- Accuracy equal or better than Doppler ABI.
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FLU AND RESPIRATORY

STATUS FLU A&B

From LifeSign

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Status Flu A & B is an in vitro rapid qualitative test that detects influenza type A and type B directly from nasal swab, nasopharyngeal swab, and nasopharyngeal aspirate/wash specimens obtained from patients with signs and symptoms of respiratory infection. It is intended to aid in the rapid differential diagnosis of Influenza A and B viral infections.

- CLIA waived *Innovative flip design with onboard sample extraction
- Premeasured developer solution capsule for increased accuracy and ease of use
- Flocked nasal swabs for improved patient comfort and superior specimen collection



STATUS COVID-19/FLU A&B PANEL TEST

From LifeSign

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A Rapid Immunoassay for the Simultaneous Direct Detection and Differential Diagnosis of SARS-CoV-2, Influenza Type A and Type B Antigen from Anterior Nasal and Nasopharyngeal swab specimens. Infections with these viruses may present similar symptoms. Can you tell them apart? WE CAN!



ACUCY INFLUENZA A&B TEST

From Sekisui Diagnostics

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The Acucy™ Influenza A&B Test is for the rapid, qualitative detection of influenza A and B viral nucleoprotein antigens from both nasal and nasopharyngeal swabs. Utilizing the Acucy™ Reader in either the point-of-care or laboratory setting, workflow flexibility is achieved with both Read Now and Walk Away features. The combination provides clinicians with standardized and definitive result interpretation.



FLU AND RESPIRATORY

METRIX® COVID-19 TEST – A MOLECULAR LAB ANYWHERE AND EVERYWHERE

From Sekisui Diagnostics

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The Metrix® COVID-19 is a novel technology includes clinical claims for symptomatic and asymptomatic individuals, along with dual-sample types for nasal or saliva, allowing for an enhanced point-of-care testing experience. The reader is compact and robust, it's ideal for professional use in diverse locations, including clinics and mobile health units. It's a maintenance free device with no calibration step required.



BE PREPARED FOR RESPIRATORY SEASONS WITH THE OSOM® COVID-19 ANTIGEN RAPID TEST

From Sekisui Diagnostics

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The OSOM® COVID-19 Antigen Rapid Test is a lateral flow immunoassay that detects the SARS-CoV-2 nucleocapsid protein with a nasal swab in only 15 minutes at the point-of-care. The test is intended to be used by healthcare professionals or operators on patients suspected of COVID-19 within the first 7 days of symptom onset. The clinical performance compares favorably against polymerase chain reaction methodology, with a positive percent agreement of 95.1% and a negative percent agreement of 97%.

OSOM® COVID-19 Antigen Rapid Test has not been FDA cleared or approved. It is authorized by FDA under an EUA for prescription use only. It has been authorized only for the detection of SARS-CoV-2 antigen, not for any other viruses or pathogens and is only authorized for the duration of the declaration that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection and/or diagnosis of COVID-19 under Section 564(b)(1) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C S360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.



CLIA WAIVED, POINT-OF-CARE, RSV TEST

From Sekisui Diagnostics

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Test for both high-risk groups, younger children & elderly adults, for severe RSV infection using the OSOM® RSV Test. This test is a CLIA-waived, point-of-care test designed to detect Respiratory Syncytial Virus (RSV) using a painless anterior nasal swab in just 15 minutes. It is suitable for both children aged 6 months to 6 years and adults aged 60 and above, providing healthcare professionals with flexibility in diagnosing patients exhibiting symptoms of respiratory infections.



HEMATOLOGY

TURN SMALL PLACES INTO SMART SPACES

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With reduced budgets, shrinking laboratory space and staffing challenges, many laboratories need a solution that lets them work smarter with less. The CELL-DYN Emerald 22 AL is a full performance, automated optical 5-part differential analyzer that delivers smarter results for small to midsize clinical laboratories.

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- Walkaway Functionality
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- Smart Safety Features



NOW IT'S MORE THANK JUST A BLOOD TEST

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With its simplified operation, the Sysmex XP-300™ is ideal for clinics and physician office labs. It provides a CBC with 17 different parameters, including a 3-part WBC Differential. The XP-300+M combines the accuracy and reliability of a Sysmex CBC with the agility of Medicus Middleware. Features include EMR connectivity, instrument interfaces and a QC module.



STATE-OF-THE-ART BENCHTOP CBC ANALYZER

From Sight Diagnostics

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OLO® by Sight Diagnostics® is a state-of-the-art benchtop CBC analyzer that leverages AI, spectroscopy, and digital fluorescent microscopy to provide lab-grade results through full blood sample digitization. OLO offers 19 CBC parameters, including a 5-part white blood cell differential and 14 distinct flags. It handles venous and capillary blood samples with a minimum of 27 µL, and is suitable for children as young as three months. OLO's unique cartridge-based technology, free from liquid reagents, and its internal controls offer easy maintenance, room-temperature storage, reduced operational overhead, and IQCP- eligibility.

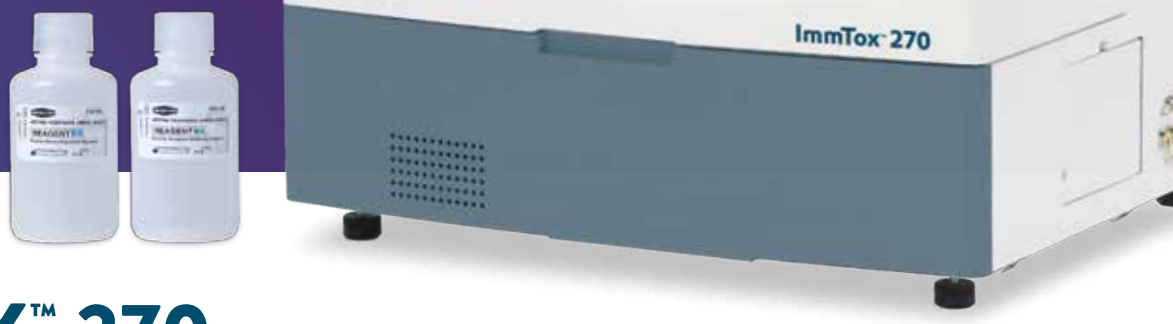
OLO is FDA 510(k) cleared for use in moderately complex laboratories. For full indications for use and safety information, please refer to the Quality and Compliance page at www.sighdx.com.



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PERIPHERAL ARTERIAL DISEASE

QUANTAFLO® PAD

From Semler Scientific

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QuantaFlo® PAD is an easy to use, accurate, point of care, non-invasive solution that aids in the early detection of peripheral arterial disease (PAD). This FDA cleared device can be administered by a medical aide in less than 5 minutes. As published in the Journal of Vascular Surgery and the American Journal of Preventive Medicine, QuantaFlo detected undiagnosed PAD in 31.6% of patients +65.1 QuantaFlo is portable and integrates with other technologies and platforms. It is ideal for both home and clinic environments.

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PAD TESTING SYSTEMS IDEAL FOR PRIMARY CARE TO VASCULAR SPECIALISTS

from Newman Medical

5624

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Your Patients Trust YOU To Find Their Peripheral Artery Disease
- High-risk patients include those over 65, diabetics, and smokers.
- If left untreated, 25% of patients with PAD will experience a heart attack or stroke within 5 years.
- PAD symptoms are often mistaken for arthritis or old age.

The simpleABI Cuff-Link System is Easy to Learn and Use.
- With a push-button remote, automatic calculations, and waveforms, it's incredibly user-friendly.
- Reports are straightforward to save and share since the system is PC-based.

Outstanding Value and Reimbursements
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- Medicare reimbursements vary by exam and location, averaging from $91 to $174.



OSOM® ULTRA STREP A TEST

From Sekisui Diagnostics

5625

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The OSOM® Ultra Strep A test is a color immunochromatographic assay intended for the qualitative detection of Group A Streptococcus antigen directly from throat swab specimens. Shown to be not statistically different than single swab culture. Sensitivity 95.7% and 100% Specificity. Includes two additional test sticks for External QC. CLIA Waived.



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2 ANS Testing

(can be combined with SUDOMOTOR into 1 full system)

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- Takes less than 10 minutes to perform, software provides verbal cues
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- **Reimburses $170/test using 3 CPT codes**
- Provides a 1 page summary up to a full 24 page comprehensive report



3 SudoMotor Testing

5628

(can be combined with ANS into 1 full system)

- Takes 3 minutes to analyze a patients' hands and feet
- Provides a 1 page summary report
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WOMEN'S HEALTH

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From Sekisui Diagnostics

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The OSOM® BVBLUE® detects elevated vaginal fluid sialidase activity, an enzyme produced by bacterial pathogens associated with bacterial vaginosis including Gardnerella, Bacteroides, Prevotella and Mobiluncus. OSOM® BVBLUE® is more sensitive than Amsel criteria providing physicians with a more accurate diagnosis to treat and minimize serious health consequences such as early spontaneous preterm births and miscarriage.



OSOM® TRICHOMONAS RAPID TEST

From Sekisui Diagnostics

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The OSOM® Trichomonas Rapid Test is intended for the qualitative detection of Trichomonas vaginalis antigens from vaginal swabs or from the saline solution. The OSOM® Trichomonas Rapid Test is a CLIA-waived rapid test available today. OSOM® Trichomonas is more sensitive than wet mount due to the assay being able to detect viable and non-viable organisms which offers significant benefits to the patient and clinician alike.



ULTRA HCG COMBO TEST

From Sekisui Diagnostics

5631

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The OSOM® Ultra hCG Combo test is a simple immunoassay for the qualitative detection of human chorionic gonadotropin (hCG) in serum or urine for the early confirmation of pregnancy. Internal studies have confirmed that the OSOM® Ultra hCG Combo test does not have a false negative result from hCG variants providing physicians with a higher level of confidence.





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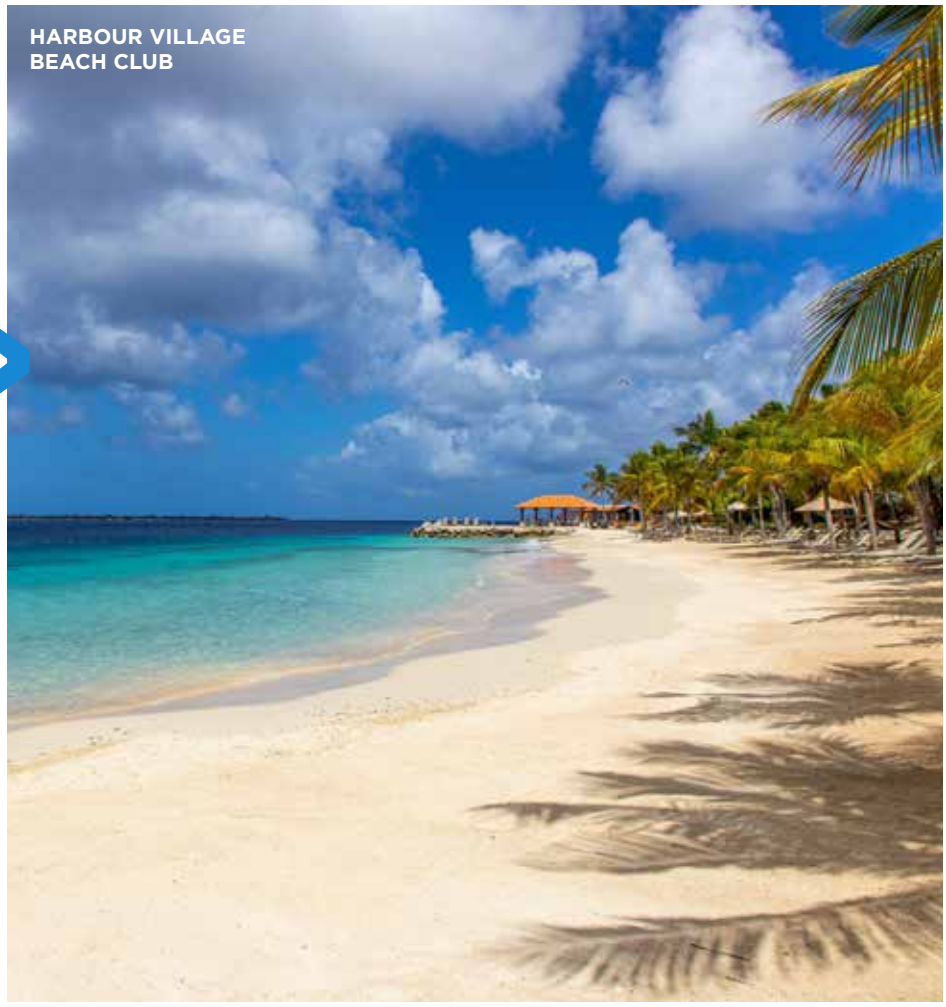
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TURTLE BAY RESORT

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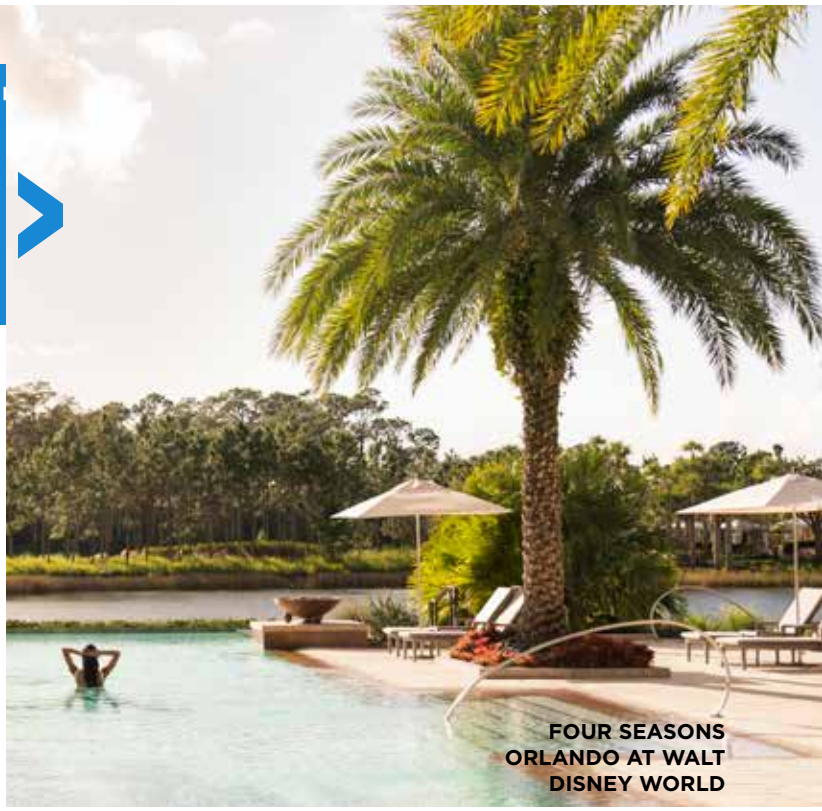
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SECRETS CAP CANA

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Balboa Bay Resort is Newport Beach's premier waterfront retreat offering stunning bay views and sunsets over Balboa Bay's harbor. It is the #1 Resort in Newport Beach per U.S. News & World Report, and it is rated as a Forbes Four-Star and AAA Four-Diamond resort.

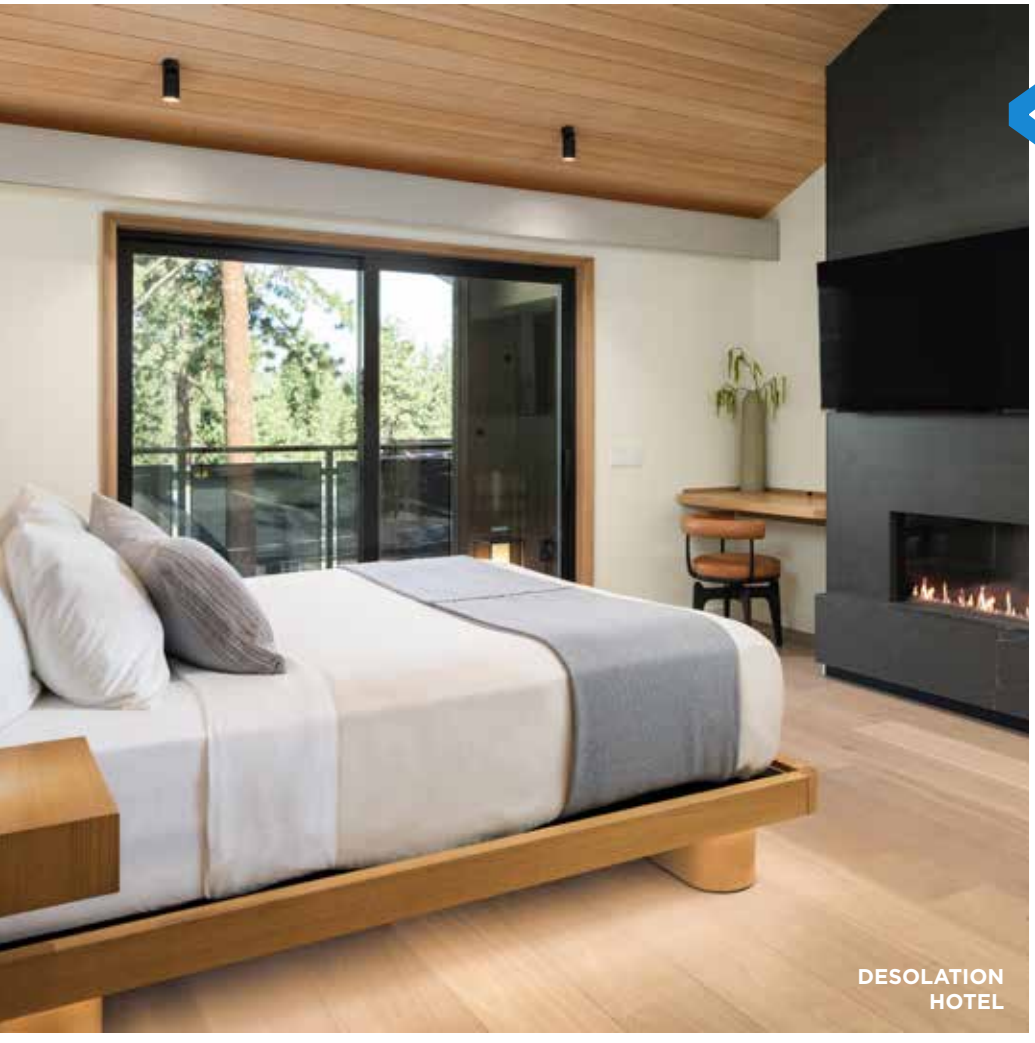
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TURTLE BAY RESORT

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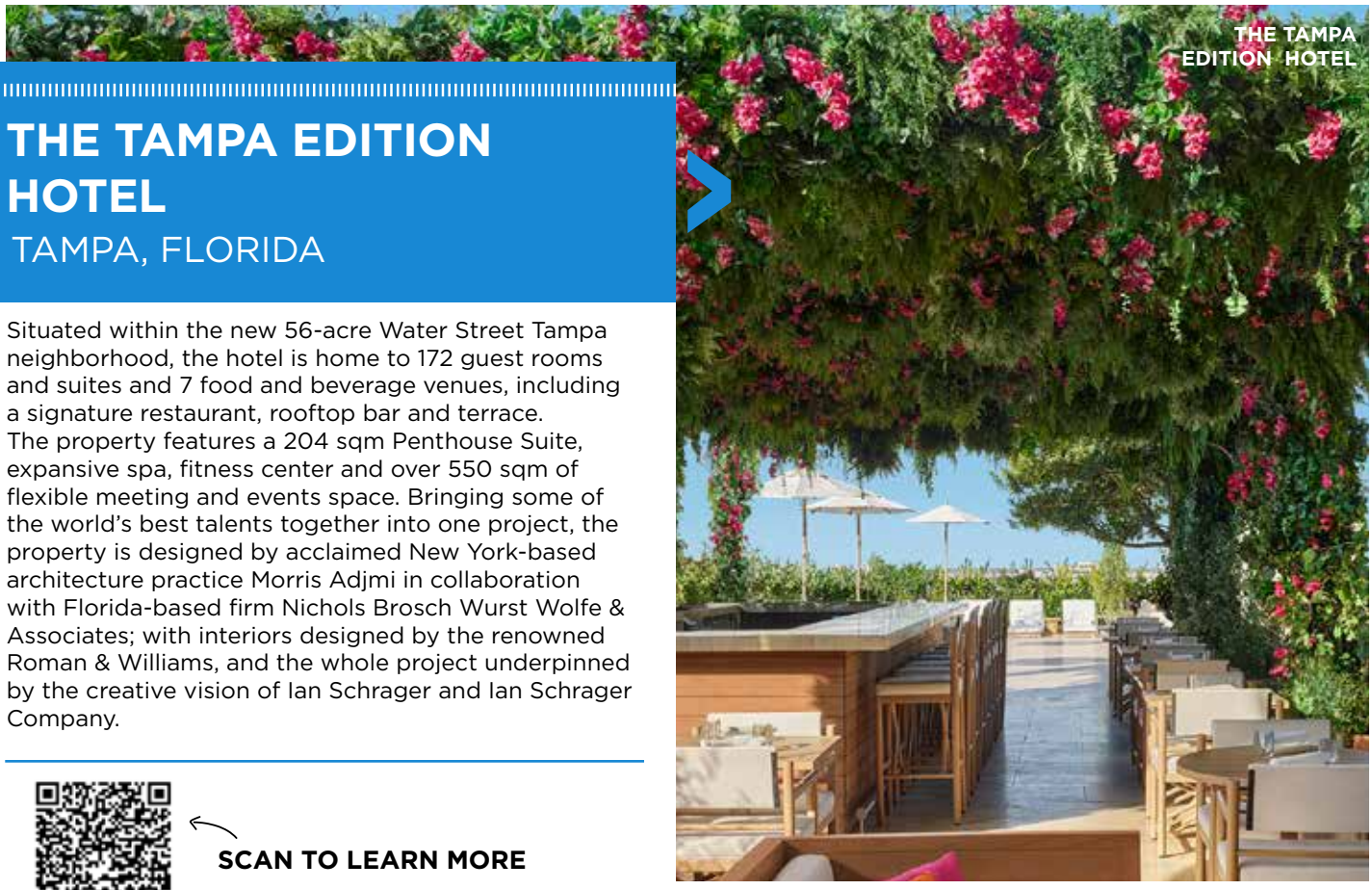
LAKE TAHOE, CALIFONIA



DESOLATION HOTEL

At Desolation Hotel, modern conveniences and eco-luxury commingle with Japanese tranquility and Scandinavian design. Our one-of-a-kind South Lake Tahoe experience inspires adventure and invites tranquility, providing the right space to recharge your battery. Balancing reverence for the past with appreciation for the present, Desolation Hotel nods to the simple days of yesteryear, while modern technology serves as a quiet backbone to the entire resort experience.

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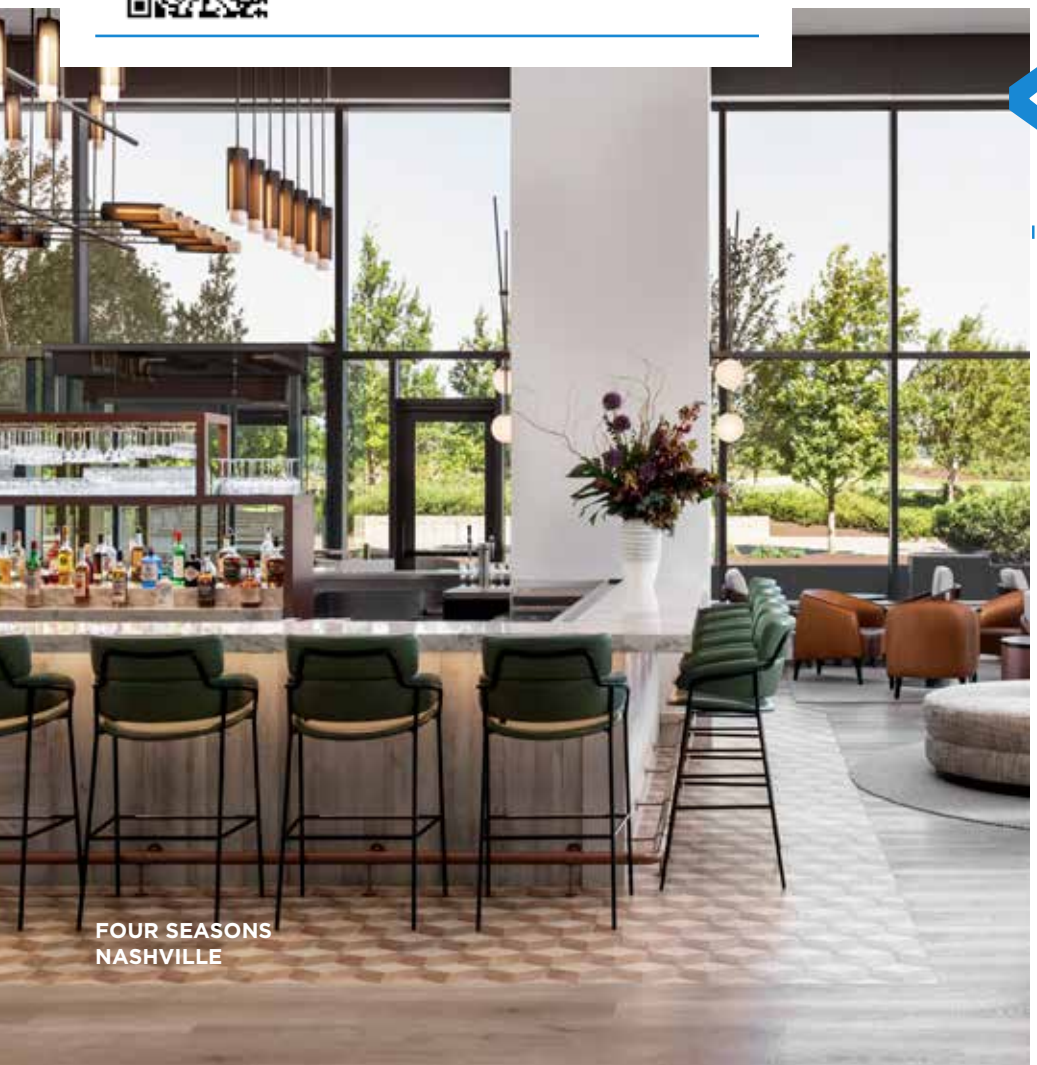
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THE TAMPA EDITION HOTEL

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Situated within the new 56-acre Water Street Tampa neighborhood, the hotel is home to 172 guest rooms and suites and 7 food and beverage venues, including a signature restaurant, rooftop bar and terrace. The property features a 204 sqm Penthouse Suite, expansive spa, fitness center and over 550 sqm of flexible meeting and events space. Bringing some of the world's best talents together into one project, the property is designed by acclaimed New York-based architecture practice Morris Adjmi in collaboration with Florida-based firm Nichols Brosch Wurst Wolfe & Associates; with interiors designed by the renowned Roman & Williams, and the whole project underpinned by the creative vision of Ian Schrager and Ian Schrager Company.

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FOUR SEASONS

NASHVILLE, TENNESSEE

Welcome to Four Seasons Hotel Nashville, a luxury hotel located in the heart of downtown's vibrant SoBro neighborhood. This new social hub is just steps away from the city's iconic music, sports, and entertainment venues. Experience the rhythm of our lively restaurants and event spaces, the tranquility of our Spa, and the stunning views from our rooftop pool overlooking the Cumberland River and Riverfront Park. With the unmatched service of Four Seasons and warm Southern hospitality, we'll inspire an authentic experience of Music City.

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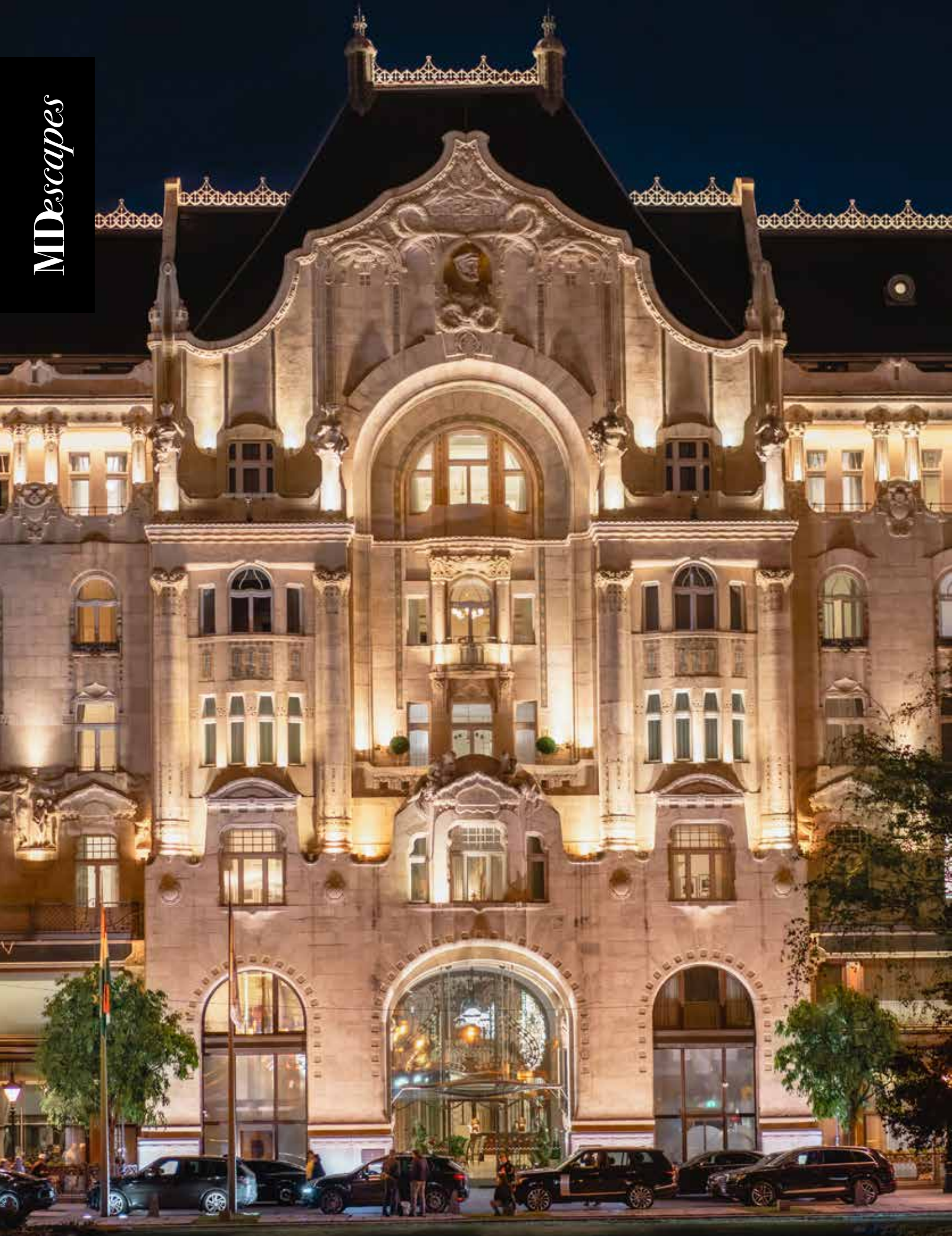
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The Palace of Hearts

FOUR SEASONS HOTEL GRESHAM PALACE BUDAPEST

A THREE-PART SERIES, BY SENIOR TRAVEL EDITOR, BRANDI BROWER

When a golden opportunity in life presents itself, you take it. You reach for the proverbial brass ring and grab it. If you get a chance to visit the Golden Triangle of Central Europe, you jump at it. An invitation to travel to three fabled capital cities —a triple threat of beauty, culture, and history —you say, "Yes, please." And you book your flight.

Budapest, Vienna, and Prague are all well-connected by efficient train routes, making them ideal for creating a seamless itinerary. These cities are also renowned for their architectural and historical offerings; forming a golden combination for a big adventure. The journey between them offers a unique opportunity to expereince the diverse culture and history of Central Europe. Add in some luxury hotels and memorable cuisine, and you have a truly epic escape, which I will share in my Golden Triangle Series over the following three issues.

First stop: Budapest.

I pride myself on not doing any research on a city I'm arriving in. Some 'A-type' personalities may view that as irresponsible, but I like the 'Ahh-ha' moments of seeing something for the first time. Budapest doesn't disappoint. It is a stunner. The Hungarian capital is comprised of two distinct parts: the Buda side and the Pest side, with the winding Danube River serving as both the divider and the connector. The Danube is the longest waterway in the EU, stretching almost 1,800 miles through ten different countries. Of all the bridges in the city, the Chain Bridge is the oldest and most iconic suspension bridge, completed in 1849, featuring stone towers and four famous lion statues that punctuate the picturesque connector. What was once destroyed in WWII was later rebuilt, recently undergoing restoration completed in 2023. It stands as a potent national symbol of Hungary, representing both unity and resilience.

Buda, or the West Bank, is the hilly side of the city, featuring scenic views and old architecture, highlighted by Buda Castle and the Castle District. Pest, or the East Bank, is the flatter and more developed side, known for its lively nightlife, grand buildings, and the National Parliament Building, which serves as a significant landmark for that side of the river. Especially beautiful at night, when all the historical buildings on both sides of the river, along with their connecting bridge, are illuminated, Budapest looks magical.

As far as "Ahh ha" moments go, if the city of Budapest is magical, then my hotel is a masterpiece. Literally, my first stay on this Golden Triangle Tour is at the iconic Four Seasons Hotel Gresham Palace, and it is easily the most historically elegant accommodation that I have ever stayed in. The building was initially constructed as an office and luxury apartments for a prominent British insurer, Gresham Life Assurance Company, in the early 1900s. The company commissioned Hungarian architect Zsigmond Quittner to design a building that would showcase the company's wealth and influence, thereby establishing a strong presence during the heyday of the Austrian-Hungarian Empire. Purchased in 1999, the Four Seasons brought the hotel's Hungarian Art Nouveau style back to life with an extensive revitalization, restoring the gorgeous historical details. Not unlike the city itself, the five-star hotel combines the refinement of yesteryear with the modern amenities of today—a sight to behold.

You never get a second chance at a first impression, a famous idiom that Four Seasons Hotel Gresham Palace has nothing to worry about. Thoroughly impressed by the entryway and lobby with its design elements straight from the La Belle Époque period ("The Beautiful Era") or the "Golden Age" of European peace and prosperity. With the elaborate metalworks of proud peacocks in silhouette, as well as stained glass and mosaic creations, the domed ceiling at the heart of the hotel is a refinement of timeless beauty. The heart of the hotel is not only the lounge area below the dome, but also the heart motif purposefully placed throughout. The nickname "the palace of hearts" is



a moniker given for the numerous hearts hidden in plain view as elements in the design—a declaration of love by the designer Zsigmond Quittner for a future resident of the palace. Discreet in design as not to distract, and yet, when they are pointed out by staff, above the elevator, part of the ceramic tiles, in the brass doors, among the stained glass windows, to name a few, you can't stop noticing.

The beautiful balance of old and new is everywhere. As I enter my room, one of 160 rooms and 19 suites, I'm struck by the wood-paneled alcove set back from the hallway, and an antique brass plate to the left, featuring a door buzzer and a slot for the magnetic keycard to be inserted—an unexpected design element. The parquet herringbone floor, high ceilings with accent stenciling, and the large window that opens up, offering a spectacular view of the Chain Bridge directly across the street, are a few standouts. The coffee station/mini bar, marble bathroom with a glass-enclosed shower and bathtub, are modern conveniences we've grown accustomed to, as is the infamous Four Seasons bed. But the little touches, the crystal ring holder on the glass shelving, the ceramic bath salts container with Gresham Palace in art deco font sitting on the edge of the tub, and sweet treats delivered daily to the room, with clever copy. My favorite was "Cube Your Enthusiasm," which included a bit of trivia about how a Hungarian visionary invented the Rubik's Cube. A confectionery block of different-flavored and colored cubes was used to replicate the six-sided enigma, a tasty surprise procured by Guest Experience Manager Ibrahim Bedran.

The excellence of the staffing should be of no surprise to anyone. It's another signature element that the brand raises the bar for others to attempt to meet. The concierge team, headed by Peter Buday, proved to be both professional and affable. The concierge area is attractive in its aesthetic, set up like a library with inviting coffee table books covering art movements and iconic Budapest. Framed, pre-war vintage posters adorn the walls, while comfy chairs and an oversized chess set round out the vibe. Levente and Balazs, two team members, are integral in planning a perfect itinerary to explore the 'Pearl of the Danube', lovingly referred to for its grandeur and elegance, like a precious pearl.

A traditional Hungarian dinner in the Jewish Quarter, at Ghetto Gulyas, was a first dip into the culture, featuring veal paprikash with baked curd and cheese noodles rolled in bacon. District VII was the perfect area to walk off our jet lag and check out the eclectic haunts of popular Budapest nightlife. Passing by the Budapest Eye, a Ferris wheel with 42 cabins, and a perfect vantage point to see the city, we stroll back to Gresham Palace.

Our first full day in Budapest begins with breakfast at the hotel's French eatery, KOLLÁZS. We sit outside to people-watch as we sip our fresh grapefruit juice and indulge in the variety of food options. Still, it's the European baked goods —chocolate brioche, fig Danish, pecan roll, and raspberry croissant — that prove difficult to pass by. The buffet offers the expected salads, fruits, cereals, and yogurts, as well as meats and cheeses, American fare items, and a selection of Hungarian foods in another section of the restaurant, if you're so inclined.

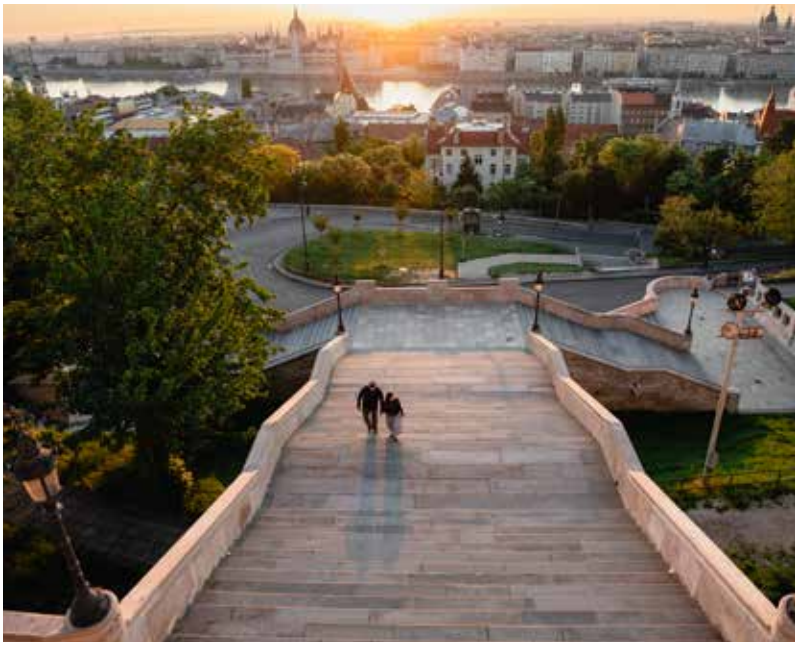
Sufficiently fueled for fun, we walk to our little neighborhood bike shop to pick up our reserved transportation for the day. The bike-friendly city provides access to several noteworthy streets and sites. The tree-lined boulevard, Andrassy Avenue, is home to the Hungarian State Opera house, luxury brand stores, and is a UNESCO World Heritage Site, known for its elegant architecture. We pedal to the end, where we enter Hero's Square, and then onto City Park. A large, red-and-white striped hot air balloon permanently anchored to the ground rises high above the park below, carrying visitors in the basket for another vantage point of the cityscape. There are several attractions in City Park, including museums, the Szechenyi Medicinal Baths, the largest thermal bath in Europe, and Vajdahunyad Castle, where an agricultural market is being held on the garden grounds. An internal debate over whether to buy paprika or creamed honey from the local farmer, so I bought both. We stop for a well-deserved ice cream after our cycling efforts and return our bikes to the shop.

We walked over the Chain Bridge, which is definitely an Instagram moment, crossing to the Buda side. We made our way to the top of Castle Hill, rather than taking the easy route via the funicular. It was there that we saw several points of interest: The Royal Palace (Buda Castle), Matthias Church, Sándor Palace, and Fisherman's Bastion. We circled to the west side of Castle Hill and made our way to the downtown area of Buda for our dinner at Stand25, a Michelin guide restaurant. We sat with a bird's-eye view of the bustling kitchen, where I enjoyed fresh sourdough bread, a spin on Caesar salad with scallops and breadcrumbs, and a lovely main course of salmon on a bed of creamy polenta and green peas. Our final destination, we walked back over the bridge to the Pest side, meeting our captain and crew member at dock 9A, where we embarked on a private Venetian-style speedboat cruise up and down the Danube River. The 50-minute ride on the water provided a different perspective of the city lights as you passed along the Buda Hills, Castle Hill, the Parliament Building, and traveled underneath the Chain Bridge, all aglow. A day of exercise, excellent food, a night-time boat ride, a comfy bed - a good night of sleep guaranteed.

Weather doesn't always work in your favor, but thanks to the preemptive efforts of a skilled concierge team, who checked the forecast and had a plan for a rainy day, we were all set. To start, how about a cozy breakfast in bed, or near our bed, with room service? Our server, Zoltan, set up the favorable fare. One of us had a foie gras omelet that was apparently "Delightful" (it wasn't me). I enjoyed the avocado toast, yogurt, and berries. For the second day in a row, I savored the best fresh grapefruit juice I've ever had and a chocolate croissant. Sometimes rainy days are the best days.

Part deux to the perfect rainy day: The Spa. Budapest, also known as "The City of Baths," owes its name to its high concentration of thermal springs and a rich history and culture of grand bathhouses dating back to the Roman and Ottoman eras. The abundant, mineral-rich waters from the deep geothermal springs offer therapeutic health benefits, as well as relaxation and socialization, a cornerstone of Hungarian culture. We





didn't have to leave our Gresham Palace to indulge in relaxation and health benefits; we just had to slip on our cozy Four Seasons robes and ride the elevator up to the top floor of the hotel. The Spa at Four Seasons Hotel Gresham Palace offers a curated selection of treatments to rejuvenate your mind and body. Before my scheduled appointment with the therapist, I soak in the serenity with The Spa amenities. I swim laps in the infinity-edge pool, adjacent to three large floor-to-ceiling windows that offer ample light despite the gray day. The whirlpool features powerful jets, followed by the steam room, where eucalyptus oil is used, and concludes with a visit to the dry sauna. I end the protocol, lounging in a chair while sipping herbal tea.



Krisztina introduces herself to me and leads me into her treatment room. A native Hungarian and 20-year veteran of her craft, she shares that she'll be performing the Touch Of The Earth treatment on me, which consists of authentic Hungarian ingredients only. She assures me that I'll look and feel relaxed and glowing after the facial. Hungarians believe the secret to staying young can be found in the land itself. She explained to me that the Earth's crust is thinner in Budapest than anywhere else in the world. The rich minerals in the thermal waters have a toning effect on the skin. As Kristina performed the rituals, it felt like four hands/twenty fingers, working on my face with rapid, unique strokes. She assured me that I'd feel the effects of her talents days after the treatment. She gave me an incredible neck and foot massage while my mask was processing. The best I've ever had! There are facials. There are European facials. And then there are facials at the Four Seasons Hotel Gresham Palace Budapest.

What could be more quintessential and cozy than an afternoon tea service in an amazing Art Nouveau lounge, in a European city, while it's raining? The Herend Afternoon Tea experience, made even more memorable by our server, Krisztian, who skillfully presents a three-tiered serving tray with tea cakes and savoury bites, as well as traditional scones, jams and clotted cream, and tea of choice served on the famous Herend Porcelain's hand-painted sets, live music via a baby grand is on an slightly elevated center stage, the pianist, as if on cue, plays softly "Once Upon a December" a beautiful piece that conjures up Anastasia and Russian Royalty imaginings. As if this day couldn't get any lovelier.

The rain tapered off, and we decided to take a stroll around the Pest side of the city, taking in lasting impressions of the side streets, statues, the historic metro trains clanging past, St. Stephan's Basilica, and the enormous Parliament building, the third-largest in the world, watching the many different-sized vessels cruising upon the waters of the Danube. As the sun begins to set, dipping down behind the silhouettes of the Castles on the Hill, we make our way back to the Chain Bridge in the heart of this city, to the stately edifice where Buda meets Pest, the Four Seasons Hotel Gresham Palace.

On our last evening, we chose to toast the town at MÚZSA, the striking lobby bar, an interesting oval-shaped space with bar stools surrounding it, and the bartenders at its center. A modern interpretation of the Art Deco movement, this creation harkens back to the opulent age of the early 20th century, with gleaming brass and a mirrored finish, allowing guests to move freely around, adding to the dynamic theatrical atmosphere, with live music playing and the special drink menu currently dedicated to "Echos of the Muses," fusing artistic mixology with mythical storytelling, innovative concoctions that bring whimsy and spirit. My companion ordered a "Gloria" that had several smoke bubbles that beckoned to be popped, which we did.

Our last meal, we dined at the hotel's KOLLÁZS, a Michelin-recommended eatery. Its name in Hungarian means "collage", and reflects its varied and creative style: a collage of cuisines, combining French flavors and touches of Hungarian specialties. And a collage of offerings: it serves as a brasserie, bar, rotisserie, wine cellar, and patisserie all in one. We begin with a shared appetizer of Heirloom Tomato with French Goat Cheese, Olive Oil, followed by Lobster Bisque with Crème Fraîche. My main course, USDA Prime Sirloin, Béarnaise, and Homemade French Fries, was not adventurous but still outstanding. Our server, Mark, was skillful in deboning and plating my companion's selection of Roasted Sea Bass, with Lemon-Garlic Sauce, as we watched tableside. The Four Seasons' Head Sommelier, Gábor Becker, was knowledgeable about Hungarian wines and offered suggestions for pairing the white fish entrée as well as a Dry Tokaji, known for its sweet flavors of honey, apricot, and peach, to complement the dessert. Our dinner was so scrumptious that there was no need to end with dessert. The entire day was a collage of experiences all within the walls of the hotel: breakfast in bed, spa treatment, afternoon tea experience, drinks at MÚZSA, followed by dinner at KOLLÁZS. That's a rainy day to remember.

As I say goodbye to this grand hotel, how were the secret hearts that were instilled into this Gresham Palace by the architect and designer received? Did the resident he longed for know they were for her? Were they lovers, or was it unrequited love? If Budapest is known as the 'Paris of the East,' and Paris is known as the 'City of Love,' the Four Seasons Hotel Gresham Palace is, by deductive reasoning, the Palace of Love. This hotel is a heartfelt love letter to the city of Budapest, where the glitter of this Art Nouveau masterpiece is resurrected, and the glow of a Golden Era remains.

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